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Dialog level 05.24.00D

Last logoff: 26feb09 14:59:34

Logon file405 27feb09 14:02:21

*** ANNOUNCEMENTS ***

*** FREE FILE OF THE MONTH: World News Connection (WNC), FILE #985
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NEW FILE

***File 651, TRADEMARKSCAN(R) - China. See HELP NEWS 651 for details.

RESUMED UPDATING

***File 523, D&B European Financial Records

RELOADS COMPLETED

***Files 154&155, MEDLINE(R)

***File 227, TRADEMARKSCAN(R) - Community Trademarks

FILES RENAMED

***File 321, PLASPEC now known as Plastic Properties Database

FILES REMOVED

***File 388,PEDS: Defense Program Summaries

***File 588,DMS-FI Contract Awards

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>>>a specific database by entering HELP NEWS <file number>. <<<

* * *

SYSTEM:HOME

Cost is in DialUnits

Menu System II: D2 version 1.8.0 term=ASCII

*** DIALOG HOMEBASE(SM) Main Menu ***

Information:

1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:

6. DIALOG(R) Document Delivery
7. Data Star(R)

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/H = Help

/L = Logoff

/NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database

(e.g., B1 for ERIC).

? b 410

27feb09 14:02:22 User226352 Session D1114.1
\$0.00 0.271 DialUnits FileHomeBase
\$0.00 Estimated cost FileHomeBase
\$0.00 Estimated cost this search
\$0.00 Estimated total session cost 0.271 DialUnits

File 410:Dialog Customer Newsletters 2008

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Set	Items	Description
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? set hi ;set hi

HIGHLIGHT set on as ''

HIGHLIGHT set on as ''

? b biochem

27feb09 14:02:33 User226352 Session D1114.2

\$0.00 0.115 DialUnits File410
\$0.00 Estimated cost File410
\$0.05 TELNET
\$0.05 Estimated cost this search
\$0.05 Estimated total session cost 0.386 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 5:Biosis Previews(R) 1926-2009/Feb W4
(c) 2009 The Thomson Corporation
File 6:NTIS 1964-2009/Mar W1
(c) 2009 NTIS, Intl Cpyrght All Rights Res
File 24:CSA Life Sciences Abstracts 1966-2009/Apr
(c) 2009 CSA.
File 34:SciSearch(R) Cited Ref Sci 1990-2009/Feb W4
(c) 2009 The Thomson Corp
File 40:Enviroline(R) 1975-2008/May
(c) 2008 Congressional Information Service
*File 40: This file is closed and will no longer update. For
similar data, please search File 76-Environmental Sciences.
File 41:Pollution Abstracts 1966-2009/May
(c) 2009 CSA.
File 45:EMCare 2009/Feb W1
(c) 2009 Elsevier B.V.
File 50:CAB Abstracts 1972-2009/Feb W4
(c) 2009 CAB International
*File 50: The file has been reloaded and accession numbers
have changed. See HELP NEWS50 for information.
File 65:Inside Conferences 1993-2009/Feb 26
(c) 2009 BLDSC all rts. reserv.
File 71:ELSEVIER BIOBASE 1994-2009/Feb W3
(c) 2009 Elsevier B.V.
*File 71: The file has been reloaded. Accession numbers
have changed.
File 72:EMBASE 1993-2009/Feb 26
(c) 2009 Elsevier B.V.
File 73:EMBASE 1974-2009/Feb 25
(c) 2009 Elsevier B.V.
File 76:Environmental Sciences 1966-2009/May
(c) 2009 CSA.
File 98:General Sci Abs 1984-2009/Jan
(c) 2009 The HW Wilson Co.
File 103:Energy SciTec 1974-2009/Jan B2
(c) 2009 Contains copyrighted material
*File 103: For access restrictions see Help Restrict.
File 136:BioEngineering Abstracts 1966-2007/Jan
(c) 2007 CSA.
*File 136: This file is closed.
File 143:Biol. & Agric. Index 1983-2009/Dec
(c) 2009 The HW Wilson Co
File 144:Pascal 1973-2009/Feb W3
(c) 2009 INIST/CNRS
File 154:MEDLINE(R) 1990-2009/Feb 20

(c) format only 2009 Dialog

*File 154: Medline has been reloaded. Please see HELP NEWS 154 for information.

File 155:MEDLINE(R) 1950-2009/Feb 20

(c) format only 2009 Dialog

*File 155: Medline has been reloaded. Please see HELP NEWS 154 for information.

File 156:ToxFile 1965-2009/Feb W4

(c) format only 2009 Dialog

File 162:Global Health 1983-2009/Feb W4

(c) 2009 CAB International

*File 162: The file has been reloaded and accession numbers have changed. See HELP NEWS 162 for information.

File 172:EMBASE Alert 2009/Feb 24

(c) 2009 Elsevier B.V.

File 305:Analytical Abstracts 1980-2009/Jan W3

(c) 2009 Royal Soc Chemistry

*File 305: Alert feature enhanced for multiple files, duplicate removal, customized scheduling. See HELP ALERT.

File 369:New Scientist 1994-2009/Feb W2

(c) 2009 Reed Business Information Ltd.

File 370:Science 1996-1999/Jul W3

(c) 1999 AAAS

*File 370: This file is closed (no updates). Use File 47 for more current information.

File 393:Beilstein Database - Abstracts 2008/Q2

(c) 2008 Beilstein GmbH

File 399:CA SEARCH(R) 1967-2009/UD=15009

(c) 2009 American Chemical Society

*File 399: Use is subject to the terms of your user/customer agreement.

IPCR/8 classification codes now searchable as IC=. See HELP NEWSIPCR.

File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec

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Set	Items	Description
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? s au=gorringe, ?		
S1	369	AU=GORRINGE, ?
? s au= reddin, ?		
S2	189	AU= REDDIN, ?
? s au=gray-owen, ?		
S3	114	AU=GRAY-OWEN, ?
? s au=boulton, ?		
S4	3106	AU=BOULTON, ?
? ds		

Set	Items	Description
S1	369	AU=GORRINGE, ?
S2	189	AU= REDDIN, ?
S3	114	AU=GRAY-OWEN, ?

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S4      3106  AU=BOULTON, ?
? s s1 or s2 or s3 or s4
      369  S1
      189  S2
      114  S3
      3106 S4
S5      3702 S1 OR S2 OR S3 OR S4
? s s5 and neisseria
      3702 S5
      143415 NEISSERIA
S6      196  S5 AND NEISSERIA
? s s5 and neisseria?
      3702 S5
      170577 NEISSERIA?
S7      198  S5 AND NEISSERIA?
? ds

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Set      Items  Description
S1        369  AU=GORRINGE, ?
S2        189  AU= REDDIN, ?
S3        114  AU=GRAY-OWEN, ?
S4        3106 AU=BOULTON, ?
S5        3702 S1 OR S2 OR S3 OR S4
S6        196  S5 AND NEISSERIA
S7        198  S5 AND NEISSERIA?
? rd s7

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>>>Duplicate detection is not supported for File 393.

>>>Records from unsupported files will be retained in the RD set.

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S8      97  RD S7 (unique items)
? s s8 and (opa or ceacam or bleb or vessicle)
      97  S8
      12195 OPA
      861  CEACAM
      14933 BLEB
      48  VESSICLE
S9      24  S8 AND (OPA OR CEACAM OR BLEB OR VESSICLE)
? t s9/7/all
>>>Format 7 is not valid in file 143

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9/7/1      (Item 1 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0003248318      IP ACCESSION NO: 8200907
CEACAM1 Dynamics during Neisseria gonorrhoeae Suppression of CD4
super(+) T Lymphocyte Activation

```

Lee, Hannah SW; Ostrowski, Mario A; Gray-Owen, Scott D
 Department of Molecular Genetics and Clinical Sciences Division,
 University

of Toronto, Toronto, Ontario, Canada

Journal of Immunology, v 180, n 10, p 6827-6835, May 2008

PUBLICATION DATE: 2008

PUBLISHER: American Association of Immunologists, 9650 Rockville Pike
Bethesda MD 20814-3998 USA, [URL:<http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0022-1767

ELECTRONIC ISSN: 1550-6606

FILE SEGMENT: Immunology Abstracts

ABSTRACT:

Neisseria gonorrhoeae colony opacity-associated (Opa) proteins bind to human carcinoembryonic antigen cellular adhesion molecules (CEACAM) found on host cells including T lymphocytes. Opa binding to CEACAM1 suppresses the activation of CD4 super(+) T cells in response to a variety of stimuli. In this study, we use primary human CD4 super(+) T cells isolated from peripheral blood to define the molecular events occurring subsequent to Opa-CEACAM1 binding. We establish that, in contrast to other cell types, T cells do not engulf *N. gonorrhoeae* upon CEACAM1 binding. Instead, the bacteria recruit CEACAM1 from intracellular stores and maintain it on the T cell surface. Upon TCR ligation, the co-engaged CEACAM1 becomes phosphorylated on tyrosine residues within the ITIMs apparent in the cytoplasmic domain. This allows the recruitment and subsequent activation of the src homology domain 2-containing tyrosine phosphatases SHP-1 and SHP-2 at the site of bacterial attachment, which prevents the normal tyrosine phosphorylation of the CD3 zeta -chain and ZAP-70 kinase in response to TCR engagement. Combined, this dynamic response allows the bacteria to effectively harness the coinhibitory function of CEACAM1 to suppress the adaptive immune response at its earliest step.

0003142661 IP ACCESSION NO: 7894419

The specific innate immune receptor CEACAM3 triggers neutrophil bactericidal activities via a Syk kinase-dependent pathway

Sarantis, Helen; Gray-Owen, Scott D
Departments of Molecular and Medical Genetics, and,
[mailto:scott.gray.owen@utoronto.ca]

Cellular Microbiology, v 9, n 9, p 2167-2180, September 2007
PUBLICATION DATE: 2007

PUBLISHER: Blackwell Publishing Ltd., 9600 Garsington Road

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 1462-5814

ELECTRONIC ISSN: 1462-5822

DOI: 10.1111/j.1462-5822.2007.00947.x

FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Immunology Abstracts

ABSTRACT:

The human-restricted pathogens *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Haemophilus influenzae* and *Moraxella catarrhalis* colonize host tissues via carcinoembryonic antigen-related cellular adhesion molecules (CEACAMs). One such receptor, CEACAM3, acts in a host-protective manner by orchestrating the capture and engulfment of invasive bacteria by human neutrophils. Herein, we show that bacterial binding to CEACAM3 causes recruitment of the cytoplasmic tyrosine kinase Syk, resulting in the phosphorylation of both CEACAM3 and Syk. This interaction is specific for the immunoreceptor tyrosine-based activation motif (ITAM) in the CEACAM3 cytoplasmic domain. While dispensable for the phagocytic uptake of single bacteria by CEACAM3, Syk is necessary for internalization when cargo size increases or when the density of CEACAM-binding ligand on the cargo surface is below a critical threshold. Moreover, Syk engagement is required for an effective bacterial killing response, including the neutrophil oxidative burst and degranulation functions in response to *N. gonorrhoeae*. These data reveal CEACAM3 as a specific innate immune receptor that mediates the opsonin-independent clearance of CEACAM-binding bacteria via Syk, a molecular trigger for functional immunoreceptor responses of both the adaptive (TCR, BCR, FcR) and innate (Dectin-1, CEACAM3) immune systems.

9/7/3 (Item 3 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0003059156 IP ACCESSION NO: 7557096
Neisserial Outer Membrane Vesicles Bind the Coinhibitory Receptor
Carcinoembryonic Antigen-Related Cellular Adhesion Molecule 1 and
Suppress
CD4 super(+) T Lymphocyte Function

Lee, Hannah SW; Boulton, Ian C; Reddin, Karen; Wong, Henry;
Halliwell, Denise; Mandelboim, Ofer; Gorringe, Andrew R;
Gray-Owen, Scott D
Department of Medical Genetics and Microbiology, University of
Toronto,
Toronto, Ontario M5S 1A8, Canada. Health Protection Agency Centre for
Emergency Preparedness and Response, Porton Down, Salisbury SP4 0JG,
United
Kingdom. The Lautenberg Center for General and Tumor Immunology,
Hadassah
Medical School, Jerusalem, Israel

Infection and Immunity, v 75, n 9, p 4449-4455, September 2007
PUBLICATION DATE: 2007

PUBLISHER: American Society for Microbiology, 1752 N Street N.W.
Washington, DC 20036 USA, [URL:<http://www.asm.org/>]

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0019-9567
ELECTRONIC ISSN: 1098-5522
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

ABSTRACT:

Pathogenic Neisseria bacteria naturally liberate outer membrane "blebs," which are presumed to contribute to pathology, and the detergent-extracted outer membrane vesicles (OMVs) from Neisseria meningitidis are currently employed as meningococcal vaccines in humans. While the composition of these vesicles reflects the bacteria from which they are derived, the functions of many of their constituent proteins remain unexplored. The neisserial colony opacity-associated Opa proteins function as adhesins, the majority of which mediate bacterial attachment to human carcinoembryonic antigen-related cellular adhesion molecules (CEACAMs). Herein, we demonstrate that the Opa proteins within OMV preparations retain the capacity to bind the immunoreceptor

tyrosine-based inhibitory motif-containing coinhibitory receptor CEACAM1.
When CD4 super(+) T lymphocytes were exposed to OMVs from Opa-expressing bacteria, their activation and proliferation in response to a variety of stimuli were effectively halted. This potent immunosuppressive effect suggests that localized infection will generate a "zone of inhibition" resulting from the diffusion of membrane blebs into the surrounding tissues. Moreover, it demonstrates that OMV-based vaccines must be developed from strains that lack CEACAM1-binding Opa variants.

9/7/4 (Item 4 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0002972103 IP ACCESSION NO: 7207958
Characterization of the *Moraxella catarrhalis* Opa-Like Protein, OlpA, Reveals a Phylogenetically Conserved Family of Outer Membrane Proteins

Brooks, Michael J; Laurence, Cassie A; Hansen, Eric J; Gray-Owen, Scott D
Department of Medical Genetics and Microbiology, University of Toronto,
Toronto, Canada M5S 1A8. Department of Microbiology, University of Texas
Southwestern Medical Center, Dallas, Texas 75390

Journal of Bacteriology, v 189, n 1, p 76-82, January 1, 2007
PUBLICATION DATE: 2007

PUBLISHER: American Society for Microbiology, 1752 N Street N.W.
Washington, DC 20036 USA, [URL:<http://www.asm.org/>]

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0021-9193
ELECTRONIC ISSN: 1098-5530
FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Genetics Abstracts

ABSTRACT:

Moraxella catarrhalis is a human-restricted pathogen that can cause respiratory tract infections. In this study, we identified a previously uncharacterized 24-kDa outer membrane protein with a high degree of similarity to *Neisseria* Opa protein adhesins, with a predicted {szligbeta}-barrel structure consisting of eight antiparallel

{szligbeta}-sheets with four surface-exposed loops. In striking contrast to the antigenically variable Opa proteins, the *M. catarrhalis* Opa-like protein (OlpA) is highly conserved and constitutively expressed, with 25 of 27 strains corresponding to a single variant. Protease treatment of intact bacteria and isolation of outer membrane vesicles confirm that the protein is surface exposed yet does not bind host cellular receptors recognized by neisserial Opa proteins. Genome-based analyses indicate that OlpA and Opa derive from a conserved family of proteins shared by a broad array of gram-negative bacteria.

9/7/5 (Item 5 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0002955456 IP ACCESSION NO: 7128392
Comparison and Correlation of Neisseria meningitidis Serogroup B Immunologic Assay Results and Human Antibody Responses following Three Doses of the Norwegian Meningococcal Outer Membrane Vesicle Vaccine MenBvac

Findlow, Jamie; Taylor, Stephen; Aase, Audun; Horton, Rachel; Heyderman, Robert; Southern, Jo; Andrews, Nick; Barchha, Rita; Harrison, Ewan; Lowe, Ann; Boxer, Emma; Heaton, Charlotte; Balmer, Paul
; Kaczmariski, Ed; Oster, Philipp; Gorringe, Andrew; Borrow, Ray; Miller, Elizabeth
Vaccine Evaluation Unit, Health Protection Agency North West, Manchester
Laboratory, Manchester Medical Microbiology Partnership, P.O. Box 209, Clinical Sciences Building II, Manchester Royal Infirmary, Manchester M13 9WZ, United Kingdom

Infection and Immunity, v 74, n 8, p 4557-4565, August 2006
PUBLICATION DATE: 2006

PUBLISHER: American Society for Microbiology, 1752 N Street N.W. Washington, DC 20036 USA, [URL:<http://www.asm.org/>]
DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0019-9567
ELECTRONIC ISSN: 1098-5522
FILE SEGMENT: Immunology Abstracts; Bacteriology Abstracts (Microbiology B)

ABSTRACT:

The prediction of efficacy of *Neisseria meningitidis* serogroup B (MenB) vaccines is currently hindered due to the lack of an appropriate correlate of protection. For outer membrane vesicle (OMV) vaccines, immunogenicity has primarily been determined by the serum bactericidal antibody (SBA) assay and OMV enzyme-linked immunosorbent assay (ELISA). However, the opsonophagocytic assay (OPA), surface labeling assay, whole blood assay (WBA), and salivary antibody ELISA have been developed although correlation with protection is presently undetermined. Therefore, the aim of the study was to investigate further the usefulness of, and relationships between, MenB immunologic assays. A phase II trial of the OMV vaccine, MenBvac, with proven efficacy was initiated to compare immunologic assays incorporating the vaccine and six heterologous strains. Correlations were achieved between the SBA assay, OMV ELISA, and OPA using human polymorphonuclear leukocytes and human complement but not between an OPA using HL60 phagocytic cells and baby rabbit complement. Correlations between the surface labeling assay, the SBA assay, and the OMV ELISA were promising, although target strain dependent. Correlations between the salivary antibody ELISA and other assays were poor. Correlations to the WBA were prevented since many samples had results greater than the range of the assay. The study confirmed the immunogenicity and benefit of a third dose of MenBvac against the homologous vaccine strain using a variety of immunologic assays. These results emphasize the need for standardized methodologies that would allow a more robust comparison of assays between laboratories and promote their further evaluation as correlates of protection against MenB disease.

9/7/6 (Item 6 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0002466930 IP ACCESSION NO: 5601270
Phosphatidylinositol 3-Kinases in Carcinoembryonic Antigen-related
Cellular
Adhesion Molecule-mediated Internalization of *Neisseria gonorrhoeae*

Booth, JW; Telio, D; Liao, EH; McCaw, SE; Matsuo, T; Grinstein, S;
Gray-Owen, SD
Division of Cell Biology, Hospital for Sick Children, Toronto,
Ontario M5G

1X8, Canada, [mailto:scott.gray.owen@utoronto.ca]

Journal of Biological Chemistry, v 278, n 16, p 14037-14045, April 18, 2003

PUBLICATION DATE: 2003

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0021-9258

DOI: 10.1074/jbc.M211879200

FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

ABSTRACT:

Neisseria gonorrhoeae can be internalized by mammalian cells through interactions between bacterial opacity-associated (Opa) adhesins and members of the human carcinoembryonic antigen-related cellular adhesion molecule (CEACAM) family. We examined the role of phosphatidylinositol 3-kinases (PI3Ks) in gonococcal invasion of epithelial cell lines expressing either CEACAM1 or CEACAM3. CEACAM3-mediated internalization, but not that mediated by CEACAM1, was accompanied by localized and transient accumulation of the class I PI3K product phosphatidylinositol 3,4,5-trisphosphate at sites of bacterial engulfment. Inhibition of phosphatidylinositol 3-kinases reduced CEACAM3-mediated uptake but, paradoxically, led to an increase in intracellular survival of bacteria internalized via either CEACAM1 or CEACAM3, suggesting additional roles for PI3K products. Consistent with this finding, the class III PI3K product phosphatidylinositol 3-phosphate accumulated and persisted in the membrane of gonococcal phagosomes after internalization. Inhibition of PI3K blocked phagosomal acquisition of the late endosomal marker lysosome-associated membrane protein 2 and reduced phagosomal acidification. Inhibiting phagosomal acidification with concanamycin A also increased survival of intracellular gonococci. These results suggest two modes of action of phosphatidylinositol 3-kinases during internalization of gonococci: synthesis of phosphatidylinositol 3,4,5-trisphosphate is important for CEACAM3-mediated uptake, while phosphatidylinositol 3-phosphate is needed for phagosomal maturation and acidification, which are required for optimal bacterial killing.

9/7/7 (Item 7 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0002402233 IP ACCESSION NO: 5711589
Immunoreceptor tyrosine-based activation motif phosphorylation during
engulfment of *Neisseria gonorrhoeae* by the neutrophil-restricted
CEACAM3 (CD66d) receptor

Mccaw, SE; Schneider, J; Liao, EH; Zimmermann, W; Gray-Owen, SD*
Department of Medical Genetics and Microbiology, University of
Toronto,
Toronto, Canada., [mailto:scott.gray.owen@utoronto.ca]

Molecular Microbiology, v 49, n 3, p 623-637, August 2003
PUBLICATION DATE: 2003

PUBLISHER: Blackwell Science Ltd

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0950-382X
DOI: 10.1046/j.1365-2958.2003.03591.x
FILE SEGMENT: Immunology Abstracts; Bacteriology Abstracts
(Microbiology B)

ABSTRACT:

Gonorrhea is characterized by a purulent urethral or cervical discharge consisting primarily of neutrophils associated with *Neisseria gonorrhoeae*. These interactions are facilitated by gonococcal colony opacity-associated (Opa) protein binding to host cellular CEACAM receptors. Of these, CEACAM3 is restricted to neutrophils and contains an immunoreceptor tyrosine-based activation motif (ITAM) reminiscent of that found within certain phagocytic Fc receptors. CEACAM3 was tyrosine phosphorylated by a Src family kinase-dependent process upon infection by gonococci expressing CEACAM-specific Opa proteins. This phosphorylation was necessary for efficient bacterial uptake; however, a less efficient uptake process became evident when kinase inhibitors or mutagenesis of the ITAM were used to prevent phosphorylation. Ligated CEACAM3 was recruited to a cytoskeleton-containing fraction, intense foci of polymerized actin were evident where bacteria attached to HeLa-CEACAM3, and disruption of polymerized actin by cytochalasin D blocked all bacterial

uptake by these cells. These data support a model whereby CEACAM3 can mediate the Opa-dependent uptake of *N. gonorrhoeae* via either an efficient, ITAM phosphorylation-dependent process that resembles phagocytosis or a less efficient, tyrosine phosphorylation-independent mechanism.

9/7/8 (Item 8 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0002333144 IP ACCESSION NO: 5388174
Neisserial binding to CEACAM1 arrests the activation and proliferation of CD4 super(+) T lymphocytes

Boulton, IC; Gray-Owen, SD
Department of Medical Genetics and Microbiology, University of Toronto,
Medical Sciences Building Rm. 4381, 1 Kings College Circle, Toronto, Ontario M5S1A8, Canada

Nature Immunology, v 3, n 3, p 229-236, March 2002
PUBLICATION DATE: 2002

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 1529-2908
DOI: 10.1038/ni769
FILE SEGMENT: Immunology Abstracts; Bacteriology Abstracts (Microbiology B)

ABSTRACT:

Infection with *Neisseria gonorrhoeae* can trigger an intense inflammatory response, yet there is little specific immune response or development of immune memory. In addition, gonorrhea typically correlates with a transient reduction in T lymphocyte counts in blood, and these populations recover when gonococcal infection is resolved. Such observations suggest that the gonococci have a suppressive effect on the host immune response. We report here that *N. gonorrhoeae* Opa proteins were able to bind CEACAM1 expressed by primary CD4 super(+) T lymphocytes and suppress their activation and proliferation. CEACAM1 bound by gonococcal Opa sub(52) associated with the tyrosine phosphatases SHP-1 and SHP-2, which implicates the receptor's ITIM (immunoreceptor tyrosine-based inhibitory motif) in this effect.

9/7/9 (Item 9 from file: 24)

DIALOG(R)File 24:CSA Life Sciences Abstracts
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0002218812 IP ACCESSION NO: 5136023
Pathogenic Neisseria Trigger Expression of Their Carcinoembryonic
Antigen-related Cellular Adhesion Molecule 1 (CEACAM1; Previously
CD66a)
Receptor on Primary Endothelial Cells by Activating the Immediate
Early
Response Transcription Factor, Nuclear Factor- Kappa B

Muenzner, P; Naumann, M; Meyer, TF; Gray-Owen, SD
Max-Planck-Institut fuer Biologie, Abteilung Infektionsbiologie,
Spemannstrasse 34, 72076 Tuebingen, Germany,
[mailto:meyer@mpiib-berlin.mpg.de]

Journal of Biological Chemistry, v 276, n 26, p 24331-24340, June 29,
2001
PUBLICATION DATE: 2001

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0021-9258
FILE SEGMENT: Nucleic Acids Abstracts; Bacteriology Abstracts
(Microbiology
B)

ABSTRACT:

Neisseria gonorrhoeae express opacity-associated (Opa)
protein adhesins that mediate binding to various members of the
carcinoembryonic antigen-related cellular adhesion molecule (CEACAM;
previously CD66) receptor family. Although human umbilical vein
endothelial
cells express little CEACAM receptor in vitro, we found
neisserial infection to induce expression of CEACAM1, CEACAM1-3L, and
CEACAM1-4L splice variants. This mediates an increased Opa
sub(52)-dependent binding of gonococci by these cells. The induced
receptor
expression did not require bacterial Opa expression, but it was more
rapid with adherent bacteria. Because the time course of induction was
similar to that seen for induced proinflammatory cytokines, we tested
whether CEACAM1 expression could be controlled by a similar mechanism.
Gonococcal infection activated a nuclear factor- Kappa B (NF- Kappa B)
heterodimer consisting of p50 and p65, and inhibitors that prevent the
nuclear translocation of activated NF- Kappa B complex inhibited
CEACAM1
transcript expression. Each of these effects could be mimicked by
using
culture filtrates or purified lipopolysaccharide instead of intact
bacteria. Together, our results support a model whereby the outer
membrane

"blebs" that are actively released by gonococci trigger a Toll-like receptor-4-dependent activation of NF- Kappa B, which up-regulates the expression of CEACAM1 to allow Opa sub(52)-mediated neisserial binding. The regulation of CEACAM1 expression by NF- Kappa B also implies a broader role for this receptor in the general inflammatory response to infection.

9/7/10 (Item 10 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0002126177 IP ACCESSION NO: 4745125
The structural basis of CEACAM-receptor targeting by neisserial Opa proteins

Billker, O; Popp, A; Gray-Owen, SD; Meyer, TF
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Trends in Microbiology, v 8, n 6, p 258-260, June 2000
PUBLICATION DATE: 2000

DOCUMENT TYPE: Journal Article; Review
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0966-842X
DOI: 10.1016/S0966-842X(00)01771-6
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

ABSTRACT:

The bacterial pathogens *Neisseria gonorrhoeae* and *Neisseria meningitidis* possess a highly polymorphic family of outer membrane proteins, the colony opacity-associated (Opa) proteins, which play a critical role in the colonization, survival, transmission and pathology of *Neisseria*. Opa-protein-mediated adhesion can result in the internalization of *Neisseria* spp. by epithelial and endothelial cells, their transcytosis across polarized epithelial monolayers and their opsonin-independent phagocytosis by professional phagocytes in vitro. Up to 11 distinct Opa proteins are encoded in unlinked chromosomal loci in gonococci, and up to four can be expressed in the meningococci. Each variant locus is subject to phase variation, resulting in a heterogeneous population of bacteria expressing none, one or several Opa proteins.

9/7/11 (Item 11 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0002102885 IP ACCESSION NO: 4734085
Carcinoembryonic antigen family receptor specificity of *Neisseria meningitidis* Opa variants influences adherence to and invasion of proinflammatory cytokine-activated endothelial cells

Muenzner, P; Dehio, Ch; Fujiwara, T; Achtman, M; Meyer, ThF*;
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Infection and Immunity, v 68, n 6, p 3601-3607, June 2000
PUBLICATION DATE: 2000

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0019-9567
DOI: 10.1128/IAI.68.6.3601-3607.2000
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

ABSTRACT:

The carcinoembryonic antigen (CEA) family member CEACAM1 (previously called biliary glycoprotein or CD66a) was previously shown to function as a receptor that can mediate the binding of Opa protein-expressing *Neisseria meningitidis* to both neutrophils and epithelial cells. Since neutrophils and polarized epithelia have both been shown to coexpress multiple CEACAM receptors, we have now extended this work to characterize the binding specificity of meningococcal Opa proteins with other CEA family members. To do so, we used recombinant *Escherichia coli* expressing nine different Opa variants from three meningococcal strains and stably transfected cell lines expressing single members of the CEACAM family. These infection studies demonstrated that seven of the nine Opa variants bound to at least one CEACAM receptor and that binding to each of these receptors is sufficient to trigger the Opa-dependent bacterial uptake by these cell lines. The other two Opa variants do not appear to bind to either CEACAM receptors or heparan sulfate proteoglycan receptors, which are bound by some gonococcal Opa variants, thus implying a novel class of Opa proteins. We have also extended previous studies by demonstrating induction

of CEACAM1 expression after stimulation of human umbilical vein endothelial cells with the proinflammatory cytokine tumor necrosis factor alpha, which is present in high concentrations during meningococcal disease. This induced expression of CEACAM1 leads to an increased Opa-dependent bacterial binding and invasion into the primary endothelia, implying that these interactions may play an important role in the pathogenesis of invasive meningococcal disease.

9/7/12 (Item 12 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0002009820 IP ACCESSION NO: 4596105
The role of neisserial Opa proteins in interactions with host cells

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Trends in Microbiology, v 6, n 12, p 489-495, December 1998
PUBLICATION DATE: 1998

DOCUMENT TYPE: Journal Article; Review
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0966-842X
DOI: 10.1016/S0966-842X(98)01365-1
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

ABSTRACT:

Pathogenic *Neisseria* spp. possess a repertoire of phase-variable Opa proteins that mediate various pathogen-host cell interactions, including bacterial engulfment by epithelial cells and opsonin-independent phagocytosis by professional phagocytes. Recent studies have identified cellular targets recognized by defined Opa proteins and have begun to reveal host signalling events involved in mediating these Opa-dependent cellular processes.

9/7/13 (Item 13 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0001937168 IP ACCESSION NO: 4443096

Opa binding to cellular CD66 receptors mediates the transcellular traversal of *Neisseria gonorrhoeae* across polarized T84 epithelial cell monolayers

Wang, J; Gray-Owen, SD; Knorre, A; Meyer, TF*; Dehio, C
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Molecular Microbiology, v 30, n 3, p 657-671, November 1998
PUBLICATION DATE: 1998

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0950-382X

FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

ABSTRACT:

We have analysed the capacity of the 11 phase-variable, opacity-associated (Opa) proteins encoded by *Neisseria gonorrhoeae* MS11 to mediate traversal across polarized monolayers of the human colonic carcinoma T84 cell line. Gonococci expressing either the heparan sulphate proteoglycan (HSPG) binding Opa protein (Opa sub(50)) or no Opa protein (Opa super(-)) did not interact with the apical pole of T84 monolayers, whereas the 10 variant Opa proteins previously shown to bind CD66 receptors were found to mediate efficient gonococcal adherence and transepithelial traversal. Consistent with this, T84 cells were shown by reverse transcriptase-polymerase chain reaction (RT-PCR) and immunoblotting to co-express CD66a (BGP), CD66c (NCA) and CD66e (CEA). The recruitment of CD66 receptors by Opa-expressing gonococci indicates their involvement in mediating adherence to the surface of T84 cells, and these bacterial interactions could be inhibited completely using polyclonal antibodies cross-reacting with all of the CD66 proteins co-expressed on T84 cells. Consistent results were obtained when Opa proteins were expressed in *Escherichia coli*, suggesting that the Opa-CD66 interaction is sufficient to mediate bacterial traversal. Transcytosis of Opa-expressing *N. gonorrhoeae* or *E. coli* did not disrupt the barrier function of infected monolayers, as indicated by a sustained transepithelial electrical resistance (TEER) throughout the course of infection, and confocal laser scanning and electron microscopy both suggest a transcellular rather than a paracellular route of traversal

across the monolayers. Parallels between the results seen here and previous work done with organ cultures confirm that T84 monolayers provide a valid model for studying neisserial interactions with the mucosal surface, and suggest that CD66 receptors contribute to this process in vivo.

9/7/14 (Item 14 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0001869001 IP ACCESSION NO: 4378973
Differential Opa specificities for CD66 receptors influence tissue interactions and cellular response to Neisseria gonorrhoeae

Gray-Owen, SD; Lorenzen, DR; Haude, A; Meyer, TF*; Dehio, C
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Spemannstrasse 34, 72076 Tuebingen, FRG

Molecular Microbiology, v 26, n 5, p 971-980, December 1997
PUBLICATION DATE: 1997

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0950-382X
FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Immunology Abstracts

ABSTRACT:

The ability of all 11 variable opacity (Opa) proteins encoded by *Neisseria gonorrhoeae* MS11 to interact directly with the five CD66 antigens was determined. Transfected HeLa cell lines expressing individual CD66 antigens were infected with recombinant *N. gonorrhoeae* and *Escherichia coli* strains expressing defined Opas. Based upon the ability of these bacteria to bind and invade and to isolate specifically CD66 antigens from detergent-soluble extracts of the corresponding cell lines, distinct specificity groups of Opa interaction with CD66 were seen. Defining these specificity groups allowed us to assign a specific function for CD66a in the Opa-mediated interaction of gonococci with two different target cell types, which are both known to co-express multiple CD66 antigens. The competence of individual Opas to interact with CD66a was strictly correlated with their ability to induce an oxidative response by polymorphonuclear neutrophils. The same Opa specificity was observed for the level of gonococcal binding to primary endothelial cells after

stimulation with TNF alpha , which was shown to increase the expression of CD66a rather than CD66e. As CD66e alone is expressed on other target tissues of gonococcal pathogenicity, Opa variation probably contributes to the cell tropism displayed by gonococci.

9/7/15 (Item 15 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0001754029 IP ACCESSION NO: 4086623
CD66 carcinoembryonic antigens mediate interactions between Opa-expressing *Neisseria gonorrhoeae* and human polymorphonuclear phagocytes

Gray-Owen, SD; Dehio, C; Haude, A; Grunert, F; Meyer, TF*
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Spemannstrasse 34, 72076 Tuebingen, Germany

EMBO Journal, v 16, n 12, p 3435-3445, June 1997
PUBLICATION DATE: 1997

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0261-4189
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

ABSTRACT:

Colonization of urogenital tissues by the human pathogen *Neisseria gonorrhoeae* is characteristically associated with purulent exudates of polymorphonuclear phagocytes (PMNs) containing apparently viable bacteria.

Distinct variant forms of the phase-variable opacity-associated (Opa) outer membrane proteins mediate the non-opsonized binding and internalization of *N. gonorrhoeae* by human PMNs. Using overlay assays and

an affinity isolation technique, we demonstrate the direct interaction between Opa sub(52)-expressing gonococci and members of the human carcinoembryonic antigen (CEA) family which express the CD66 epitope. Gonococci and recombinant *Escherichia coli* strains synthesizing Opa sub(52) showed specific binding and internalization by transfected HeLa

cell lines expressing the CD66 family members BGP (CD66a), NCA (CD66c),

CGM1 (CD66d) and CEA (CD66e), but not that expressing CGM6 (CD66b). Bacterial strains expressing either no opacity protein or the epithelial

cell invasion-associated Opa sub(50) do not bind these CEA family members. Consistent with their different receptor specificities, Opa

sub(52)-mediated interactions could be inhibited by polyclonal anti-CEA sera, while Opa sub(50) binding was instead inhibited by heparin. Using confocal laser scanning microscopy, we observed a marked recruitment of CD66 antigen by Opa sub(52)-expressing gonococci on both the transfected cell lines and infected PMNs. These data indicate that members of the CEA family constitute the cellular receptors for the interaction with, and internalization of, *N. gonorrhoeae*.

9/7/16 (Item 1 from file: 65)
DIALOG(R)File 65:Inside Conferences
(c) 2009 BLDSC all rts. reserv. All rts. reserv.

03897593 INSIDE CONFERENCE ITEM ID: CN040958307
The outcome of neisserial Opa-mediated binding depends upon target cell type and its expressed CD66 receptor repertoire
Gray-Owen, S. D.; Dehio, C.; Popp, A.; Wang, J.; Munzner, P.; Hauck, C.; Gulbins, E.; Grunert, F.; Zimmerman, W.; Meyer, T. F.
CONFERENCE: International pathogenic Neisseria conference-11th
ABSTRACTS OF THE INTERNATIONAL PATHOGENIC NEISSERIA CONFERENCE , 1998;
11TH P: 34
Paris, EDK, 1998
ISBN: 2842540158
LANGUAGE: English DOCUMENT TYPE: Conference Selected abstracts
CONFERENCE LOCATION: Nice, France 1998; Nov (199811)

9/7/17 (Item 1 from file: 162)
DIALOG(R)File 162:Global Health
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0004960541 CAB Accession Number: 20033190008
Neisserial Opa proteins: impact on colonization, dissemination and immunity.
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Conference Title: Proceedings of Nobel Symposium Number 124, Septicemia and Shock: Pathogenesis and Novel Therapeutic Strategies, Stockholm, Sweden. 15-17 May 2003.
Scandinavian Journal of Infectious Diseases volume 35 (9): p.614-618

Publication Year: 2003
ISSN: 0036-5548
Digital Object Identifier: 10.1080/00365540310016042
Publisher: Taylor & Francis Ltd Basingstoke, UK
Language: English
Record Type: Abstract
Document Type: Journal article; Conference paper

The pathogenic *Neisseria* sp. encode a family of phase-variable and antigenically distinct Opa proteins that allow bacterial attachment to virtually every cell type encountered during infection. Some Opa variants bind cell surface-expressed heparan sulfate proteoglycans, including members of the syndecan family of receptors, and extracellular matrix proteins such as fibronectin and vitronectin. Other variants bind members of the carcinoembryonic antigen family of cellular adhesion molecules. Depending on the Opa variant(s) expressed, these receptor interactions can allow neisserial entry and transcellular transcytosis across polarized epithelial cell monolayers, entry into endothelial cells, suppression of lymphocyte function and/or bacterial engulfment and killing by neutrophils. Recent advances in our understanding of how these Opa protein-mediated interactions influence the host cellular response are discussed in the context of their impact on various stages of neisserial infection.

55 reference

9/7/18 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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149264841 CA: 149(12)264841q JOURNAL
Characterization of the key antigenic components and pre-clinical immune responses to a meningococcal disease vaccine based on *Neisseria lactamica* outer membrane vesicle
AUTHOR(S): Finney, Michelle; Vaughan, Thomas; Taylor, Stephen; Hudson, Michael J.; Pratt, Catherine; Wheeler, Jun X.; Vipond, Caroline; Feavers, Ian; Jones, Christopher; Findlow, Jamie; Borrow, Ray; Gorringe, Andrew
LOCATION: Centre for Emergency Preparedness and Response, Health Protection Agency, Porton Down, Salisbury, UK,
JOURNAL: Hum. Vaccines (Human Vaccines) DATE: 2008 VOLUME: 4
NUMBER: 1

PAGES: 23-30 CODEN: HVUAAK ISSN: 1554-8600 LANGUAGE: English

PUBLISHER: Landes Bioscience

SECTION:

CA215002 Immunochemistry

IDENTIFIERS: Neisseria outer membrane vesicle vaccine IgG

opsonophagocytosis meningococcal disease

DESCRIPTORS:

Proteins...

adhesion and penetration; characterization of key antigenic components

and pre-clin. immune responses to meningococcal disease vaccine based

on Neisseria lactamica outer membrane vesicles

Human... Neisseria lactamica... Neisseria meningitidis... Vaccines...

characterization of key antigenic components and pre-clin. immune

responses to meningococcal disease vaccine based on Neisseria

lactamica

outer membrane vesicles

Proteins...

FrpB; characterization of key antigenic components and pre-clin. immune

responses to meningococcal disease vaccine based on Neisseria

lactamica

outer membrane vesicles

Proteins...

HpuB; characterization of key antigenic components and pre-clin. immune

responses to meningococcal disease vaccine based on Neisseria

lactamica

outer membrane vesicles

Antibodies and Immunoglobulins...

IgG; characterization of key antigenic components and pre-clin. immune

responses to meningococcal disease vaccine based on Neisseria

lactamica

outer membrane vesicles

Proteins...

LbpA; characterization of key antigenic components and pre-clin. immune

responses to meningococcal disease vaccine based on Neisseria

lactamica

outer membrane vesicles

Disease, animal...

meningococcal; characterization of key antigenic components and

pre-clin. immune responses to meningococcal disease vaccine based on

Neisseria lactamica outer membrane vesicles

Proteins...

NspA; characterization of key antigenic components and pre-clin. immune

responses to meningococcal disease vaccine based on Neisseria

lactamica

outer membrane vesicles
Proteins...
OmpP1; characterization of key antigenic components and pre-clin.
immune responses to meningococcal disease vaccine based on
Neisseria
lactamica outer membrane vesicles
Proteins...
Omp85; characterization of key antigenic components and pre-clin.
immune responses to meningococcal disease vaccine based on
Neisseria
lactamica outer membrane vesicles
Proteins...
Opa; characterization of key antigenic components and pre-clin.
immune
responses to meningococcal disease vaccine based on Neisseria
lactamica
outer membrane vesicles
Phagocytosis...
opsonophagocytosis; characterization of key antigenic components
and
pre-clin. immune responses to meningococcal disease vaccine based
on
Neisseria lactamica outer membrane vesicles
Cell wall...
outer membrane; characterization of key antigenic components and
pre-clin. immune responses to meningococcal disease vaccine based
on
Neisseria lactamica outer membrane vesicles
Proteins...
PilQ; characterization of key antigenic components and pre-clin.
immune
responses to meningococcal disease vaccine based on Neisseria
lactamica
outer membrane vesicles
Proteins...
PorB; characterization of key antigenic components and pre-clin.
immune
responses to meningococcal disease vaccine based on Neisseria
lactamica
outer membrane vesicles
Proteins...
PrlC; characterization of key antigenic components and pre-clin.
immune
responses to meningococcal disease vaccine based on Neisseria
lactamica
outer membrane vesicles
Proteins...
RmpM; characterization of key antigenic components and pre-clin.
immune
responses to meningococcal disease vaccine based on Neisseria
lactamica
outer membrane vesicles

Proteins...

RpsC; characterization of key antigenic components and pre-clin.
immune

responses to meningococcal disease vaccine based on Neisseria
lactamica

outer membrane vesicles

Proteins...

TbpA; characterization of key antigenic components and pre-clin.
immune

responses to meningococcal disease vaccine based on Neisseria
lactamica

outer membrane vesicles

9/7/19 (Item 2 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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147275509 CA: 147(13)275509x JOURNAL

Neisserial outer membrane vesicles bind the coinhibitory receptor
carcinoembryonic antigen-related cellular adhesion molecule 1 and
suppress CD4+ T lymphocyte function

AUTHOR(S): Lee, Hannah S. W.; Boulton, Ian C.; Reddin, Karen; Wong,
Henry
; Halliwell, Denise; Mandelboim, Ofer; Gorringe, Andrew R.; Gray-Owen,
Scott D.

LOCATION: Department of Medical Genetics and Microbiology,
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JOURNAL: Infect. Immun. (Infection and Immunity) DATE: 2007
VOLUME: 75

NUMBER: 9 PAGES: 4449-4455 CODEN: INFIBR ISSN: 0019-9567

LANGUAGE:

English PUBLISHER: American Society for Microbiology

SECTION:

CA215008 Immunochemistry

IDENTIFIERS: Neisseria OMV Opa protein CEACAM1 CD4 T cell
immunosuppression

DESCRIPTORS:

T cell(lymphocyte)...

activation; neisserial outer membrane vesicles (OMV) containing

Opa

proteins bind CEACAM1 mol. and suppress CD4+ T lymphocyte function

Glycoproteins...

BGP I (biliary glycoprotein I); neisserial outer membrane vesicles
(OMV) containing Opa proteins bind CEACAM1 mol. and suppress CD4+

T

lymphocyte function

CD4-positive T cell... Human... Immunosuppression... Neisseria
meningitidis

... Neisseria...

neisserial outer membrane vesicles (OMV) containing Opa proteins
bind

CEACAM1 mol. and suppress CD4+ T lymphocyte function
Adhesins...

Opa (opacity-associated); neisserial outer membrane vesicles
(OMV) containing

Opa proteins bind CEACAM1 mol. and suppress CD4+ T lymphocyte
function
Cell wall...

outer membrane; neisserial outer membrane vesicles (OMV)
containing Opa
proteins bind CEACAM1 mol. and suppress CD4+ T lymphocyte function
T cell(lymphocyte)...

proliferation; neisserial outer membrane vesicles (OMV)
containing Opa
proteins bind CEACAM1 mol. and suppress CD4+ T lymphocyte function

9/7/20 (Item 3 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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142372478 CA: 142(20)372478r PATENT

Modified whole cell, cell extract, and OMV (outer membrane
vesicle)-based

vaccines for treatment or prevention of disease caused by Gram-neg.
bacteria

INVENTOR(AUTHOR): Gorringer, Andrew R.; Reddin, Karen M.; Gray-Owen,
Scott

D.; Boulton, Ian C.

LOCATION: UK,

ASSIGNEE: Health Protection Agency

PATENT: PCT International ; WO 200535733 A2 DATE: 20050421

APPLICATION: WO 2004GB4274 (20041008) *GB 200323709 (20031009)

PAGES: 35 pp. CODEN: PIXXD2 LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: C12N-001/00A

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR;
BW; BY;

BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; EG; ES; FI;
GB; GD;

GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK;
LR; LS;

LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NA; NI; NO; NZ; OM; PG;
PH; PL;

PT; RO; RU; SC; SD; SE; SG; SK; SL; SY; TJ; TM; TN; TR; TT; TZ; UA;
UG; US;

UZ; VC; VN; YU; ZA; ZM; ZW DESIGNATED REGIONAL: BW; GH; GM; KE; LS;
MW; MZ

; NA; SD; SL; SZ; TZ; UG; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM;
AT;

BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HU; IE; IT; LU;
MC; NL;

PL; PT; RO; SE; SI; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW;
ML; MR;

NE; SN; TD; TG

SECTION:

CA215002 Immunochemistry

CA263XXX Pharmaceuticals

IDENTIFIERS: vaccine Gram neg bacterial infection Neisseria

DESCRIPTORS:

T cell(lymphocyte)...

activation; modified whole cell, cell extract, and OMV (outer membrane vesicle)-based vaccines for treatment or prevention of disease caused by Gram-neg. bacteria

Glycoproteins...

BGP I (biliary glycoprotein I); modified whole cell, cell extract, and OMV (outer membrane vesicle)-based vaccines (free of Opa protein that binds CEACAM1) for treatment or prevention of disease caused b

Drug delivery systems...

carriers; modified whole cell, cell extract, and OMV (outer membrane vesicle)-based vaccines for treatment or prevention of disease caused by Gram-neg. bacteria

Vaccines... Gram-negative bacteria... Neisseria... Moraxella... Kingella...

Acinetobacter... Brucella... Bordetella... Porphyromonas...

Actinobacillus

... Borrelia... Serratia... Campylobacter... Helicobacter...

Haemophilus...

Escherichia... Legionella... Salmonella... Pseudomonas... Yersinia...

Neisseria meningitidis... Neisseria gonorrhoeae... CD4-positive T cell...

Mutation... Mutagenesis... Antigens... Antibodies and Immunoglobulins...

Gene,microbial... Genetic vectors... Human... Neisseria lactamica... modified whole cell, cell extract, and OMV (outer membrane vesicle)-based

vaccines for treatment or prevention of disease caused by Gram-neg. bacteria

Proteins...

Op (opacity protein); modified whole cell, cell extract, and OMV (outer membrane vesicle)-based vaccines (free of Opa protein that binds CEACAM1) for treatment or prevention of disease caused by Gram-neg Organelle...

outer membrane vesicle (OMV); modified whole cell, cell extract, and OMV

(outer membrane vesicle)-based vaccines for treatment or prevention of disease caused by Gram-neg. bacteria

T cell(lymphocyte)...

proliferation; modified whole cell, cell extract, and OMV (outer membrane

vesicle)-based vaccines for treatment or prevention of disease caused

by Gram-neg. bacteria

CAS REGISTRY NUMBERS:

62-50-0 EMS and NTG use to induce mutagenesis in *Neisseria meningitidis*

for vaccine preparation

674-81-7 modified whole cell, cell extract, and OMV (outer membrane vesicle)-based vaccines for treatment or prevention of disease caused

by Gram-neg. bacteria

9/7/21 (Item 4 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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140390199 CA: 140(24)390199p JOURNAL

Engulfment of *Neisseria gonorrhoeae*: Revealing distinct processes of bacterial entry by individual carcinoembryonic antigen-related cellular

adhesion molecule family receptors

AUTHOR(S): McCaw, Shannon E.; Liao, Edward H.; Gray-Owen, Scott D.

LOCATION: Department of Medical Genetics and Microbiology, University of

Toronto, Toronto, ON, Can., M5S 1A8

JOURNAL: Infect. Immun. (Infection and Immunity) DATE: 2004
VOLUME: 72

NUMBER: 5 PAGES: 2742-2752 CODEN: INFIBR ISSN: 0019-9567

LANGUAGE:

English PUBLISHER: American Society for Microbiology

SECTION:

CA215008 Immunochemistry

IDENTIFIERS: *Neisseria* entry carcinoembryonic antigen related adhesion

mol receptor

DESCRIPTORS:

Receptors...

CEACAM; *Neisseria gonorrhoeae* engulfment by individual carcinoembryonic

antigen-related cellular adhesion mol. family receptors

Carcinoembryonic antigen... HeLa cell... Human... *Neisseria gonorrhoeae*...

Neisseria gonorrhoeae engulfment by individual carcinoembryonic

antigen-related cellular adhesion mol. family receptors

Proteins...

Opa; *Neisseria gonorrhoeae* engulfment by individual carcinoembryonic

antigen-related cellular adhesion mol. family receptors

Organelle...

phagosome; Neisseria gonorrhoeae engulfment by individual
carcinoembryonic antigen-related cellular adhesion mol. family
receptors

9/7/22 (Item 5 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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138131109 CA: 138(10)131109h PATENT

Ligation of CEACAM1 using a neisserial Opa protein, and methods for
immune response suppression and inhibition of tumor cell growth

INVENTOR(AUTHOR): Gray-Owen, Scott D.; Boulton, Ian C.

LOCATION: Can.,

PATENT: U.S. Pat. Appl. Publ. ; US 20030022292 A1 DATE: 20030130

APPLICATION: US 163638 (20020607) *US PV296152 (20010607)

PAGES: 48 pp. CODEN: USXXCO LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: 435069100; C12P-021/06A; A61K-039/00B; A61K-039/38B

SECTION:

CA201007 Pharmacology

CA215XXX Immunochemistry

IDENTIFIERS: immunosuppression CEACAM1 ligation neisserial Opa
protein,

tumor inhibition CEACAM1 ligation neisserial Opa protein

DESCRIPTORS:

CD3(antigen)... Lymphocyte...

activation; CEACAM1 ligation using bacterial protein, and methods
for

immune response suppression and inhibition of tumor cell growth

Proteins...

bacterial; CEACAM1 ligation using bacterial protein, and methods
for

immune response suppression and inhibition of tumor cell growth

Glycoproteins...

BGP I (biliary glycoprotein I); CEACAM1 ligation using neisserial
Opa

protein, and methods for immune response suppression and
inhibition of

tumor cell growth

Cytotoxic agents...

CD4+ T-lymphocyte proliferation inhibition; CEACAM1 ligation using
bacterial protein, and methods for immune response suppression and
inhibition of tumor cell growth

Antibodies...

CEACAM-specific; CEACAM1 ligation using bacterial protein, and
methods

for immune response suppression and inhibition of tumor cell
growth

Haemophilus... T cell(lymphocyte)... B cell(lymphocyte)... Dendritic
cell

... CD4-positive T cell... Autoimmune disease... Transplant rejection...
Allergy... Allergy inhibitors... Inflammation... Anti-inflammatory agents
... Neoplasm... Antitumor agents... Interleukin 2... Neisseria gonorrhoeae
... Human... CD28(antigen)... CD69(antigen)...
CEACAM1 ligation using bacterial protein, and methods for immune response suppression and inhibition of tumor cell growth
Immunomodulators... Immunosuppressants... Immunostimulants... Neisseria...
CEACAM1 ligation using neisserial Opa protein, and methods for immune response suppression and inhibition of tumor cell growth
Embryo, animal...
fetus, fetal loss; CEACAM1 ligation using bacterial protein, and methods for immune response suppression and inhibition of tumor cell growth
Transplant and Transplantation...
graft-vs.-host reaction; CEACAM1 ligation using bacterial protein, and methods for immune response suppression and inhibition of tumor cell growth
T cell(lymphocyte)...
helper cell; CEACAM1 ligation using bacterial protein, and methods for immune response suppression and inhibition of tumor cell growth
Proteoglycans, biological studies...
heparitin sulfate-containing, HSPG-specific Opa50 variant; CEACAM1 ligation using bacterial protein, and methods for immune response suppression and inhibition of tumor cell growth
Proteins...
HSPG-specific Opa50 variant; CEACAM1 ligation using bacterial protein, and methods for immune response suppression and inhibition of tumor cell growth
Animal cell line...
JURKAT; CEACAM1 ligation using bacterial protein, and methods for immune response suppression and inhibition of tumor cell growth
Cell activation...
lymphocyte; CEACAM1 ligation using bacterial protein, and methods for immune response suppression and inhibition of tumor cell growth
Lymphocyte...
natural killer cell; CEACAM1 ligation using bacterial protein, and methods for immune response suppression and inhibition of tumor cell

growth
 Proteins...
 Opa; CEACAM1 ligation using bacterial protein, and methods for
 immune
 response suppression and inhibition of tumor cell growth
 Proteins...
 Opa52; CEACAM1 ligation using bacterial protein, and methods for
 immune
 response suppression and inhibition of tumor cell growth
 Proteins...
 Opa57; CEACAM1 ligation using bacterial protein, and methods for
 immune
 response suppression and inhibition of tumor cell growth
 T cell(lymphocyte)...
 proliferation; CEACAM1 ligation using bacterial protein, and
 methods
 for immune response suppression and inhibition of tumor cell
 growth
 Bacteria(Eubacteria)...
 proteins; CEACAM1 ligation using bacterial protein, and methods
 for
 immune response suppression and inhibition of tumor cell growth
 Cell proliferation...
 T cell; CEACAM1 ligation using bacterial protein, and methods for
 immune response suppression and inhibition of tumor cell growth
 CAS REGISTRY NUMBERS:
 300855-77-0 301156-53-6 Opa52-bound CEACAM1 association with;
 CEACAM1
 ligation using bacterial protein, and methods for immune response
 suppression and inhibition of tumor cell growth
 491896-02-7 491896-03-8 491896-04-9 491896-05-0 491896-06-1
 491896-07-2 491896-08-3 491896-09-4 491896-10-7 491896-11-8
 491896-12-9 491896-13-0 491896-14-1 491896-15-2 unclaimed
 nucleotide sequence; ligation of CEACAM1 using a neisserial Opa
 protein, and methods for immune response suppression and
 inhibition of
 tumor cell growth
 491923-34-3 491923-35-4 unclaimed protein sequence; ligation of
 CEACAM1
 using a neisserial Opa protein, and methods for immune response
 suppression and inhibition of tumor cell growth
 491896-16-3 491896-17-4 unclaimed sequence; ligation of CEACAM1
 using a
 neisserial Opa protein, and methods for immune response
 suppression and
 inhibition of tumor cell growth

136323642 CA: 136(21)323642g JOURNAL
 Neisserial binding to CEACAMI arrests the activation and
 proliferation of
 CD4+ T lymphocytes
 AUTHOR(S): Boulton, Ian C.; Gray-Owen, Scott D.
 LOCATION: Department of Medical Genetics and Microbiology,
 University of
 Toronto, Toronto, ON, Can., M5S 1A8
 JOURNAL: Nat. Immunol. DATE: 2002 VOLUME: 3 NUMBER: 3 PAGES:
 229-236
 CODEN: NIAMCZ ISSN: 1529-2908 LANGUAGE: English PUBLISHER: Nature
 America Inc.
 SECTION:
 CA215002 Immunochemistry
 CA214XXX Mammalian Pathological Biochemistry
 IDENTIFIERS: Neisserial CEACAMI Opa protein gonorrhoeae T lymphocyte
 phosphatase
 DESCRIPTORS:
 Cell adhesion molecules...
 CEACAM1 (carcinoembryonic antigen-related cellular adhesion mol.
 1);
 neisserial binding to CEACAMI arrests activation and
 proliferation of
 CD4+ T lymphocytes
 Sexually transmitted diseases...
 gonorrhea; neisserial binding to CEACAMI arrests activation and
 proliferation of CD4+ T lymphocytes
 Cell proliferation...
 inhibition; neisserial binding to CEACAMI arrests activation and
 proliferation of CD4+ T lymphocytes
 Protein motifs...
 ITIM (immunoreceptor tyrosine-based inhibitory motif); neisserial
 binding to CEACAMI arrests activation and proliferation of CD4+ T
 lymphocytes
 Apoptosis... CD4-positive T cell... Human... Immunosuppressants...
 Neisseria gonorrhoeae...
 neisserial binding to CEACAMI arrests activation and
 proliferation of
 CD4+ T lymphocytes
 Proteins...
 Opa52; neisserial binding to CEACAMI arrests activation and
 proliferation of CD4+ T lymphocytes
 Cell activation...
 T cell; neisserial binding to CEACAMI arrests activation and
 proliferation of CD4+ T lymphocytes
 CAS REGISTRY NUMBERS:
 300855-77-0 301156-53-6 neisserial binding to CEACAMI arrests
 activation
 and proliferation of CD4+ T lymphocytes

DIALOG(R)File 399:CA SEARCH(R)

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132263379 CA: 132(20)263379g JOURNAL

Molecular analysis of neisserial Opa protein interactions with the
CEA

family of receptors: identification of determinants contributing to
the

differential specificities of binding

AUTHOR(S): Popp, Andreas; Dehio, Christoph; Grunert, Fritz; Meyer,
Thomas

F.; Gray-Owen, Scott D.

LOCATION: Max-Planck-Institut fur Biologie, Abteilung
Infektionsbiologie,

Tubingen, Germany, D-72076

JOURNAL: Cell. Microbiol. DATE: 1999 VOLUME: 1 NUMBER: 2 PAGES:
169-181 CODEN: CEMIF5 ISSN: 1462-5814 LANGUAGE: English PUBLISHER:
Blackwell Science Ltd.

SECTION:

CA214003 Mammalian Pathological Biochemistry

CA210XXX MICROBIAL, ALGAL, AND FUNGAL BIOCHEMISTRY

IDENTIFIERS: Neisserial Opa protein binding CEA receptor structure
DESCRIPTORS:

CD antigens...

CD66, CEACAM1; structural features of CEA gene family proteins in
binding to neisserial Opa proteins

Proteins,specific or class...

CEACAM4; absence of neisserial Opa proteins binding to

Proteins,specific or class...

CEACAM7; absence of neisserial Opa proteins binding to

Antigens...

NCA (nonspecific crossreactive antigen); structural features of

CEA

gene family proteins in binding to neisserial Opa proteins

Protein motifs...

of CEA gene family proteins in binding to neisserial Opa proteins

Molecular association...

of CEA gene family proteins with neisserial Opa proteins

Proteins,specific or class...

Op (opacity protein); structural features of CEA gene family

proteins

in binding to

Carcinoembryonic antigen...

structural features of CEA gene family proteins in binding to

neisserial Opa proteins

Neisseria gonorrhoeae...

structural features of CEA gene family proteins in binding to Opa

proteins of

? ds

Set	Items	Description
S1	369	AU=GORRINGE, ?

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S2      189    AU= REDDIN, ?
S3      114    AU=GRAY-OWEN, ?
S4      3106   AU=BOULTON, ?
S5      3702   S1 OR S2 OR S3 OR S4
S6      196    S5 AND NEISSERIA
S7      198    S5 AND NEISSERIA?
S8      97     RD S7 (unique items)
S9      24     S8 AND (OPA OR CEACAM OR BLEB OR VESSICLE)
? s ceadam and opa and neisseria?
      0 CEADAM
      12195 OPA
      170577 NEISSERIA?
      S10      0 CEADAM AND OPA AND NEISSERIA?
? s ceacam? and opa and neisseria?
      3755 CEACAM?
      12195 OPA
      170577 NEISSERIA?
      S11      368 CEACAM? AND OPA AND NEISSERIA?
? rd s11

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>>>Duplicate detection is not supported for File 393.

>>>Records from unsupported files will be retained in the RD set.

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S2	189	AU= REDDIN, ?
S3	114	AU=GRAY-OWEN, ?
S4	3106	AU=BOULTON, ?
S5	3702	S1 OR S2 OR S3 OR S4
S6	196	S5 AND NEISSERIA
S7	198	S5 AND NEISSERIA?
S8	97	RD S7 (unique items)
S9	24	S8 AND (OPA OR CEACAM OR BLEB OR VESSICLE)
S10	0	CEADAM AND OPA AND NEISSERIA?
S11	368	CEACAM? AND OPA AND NEISSERIA?
S12	74	RD S11 (unique items)
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	74	S12
	24	S9
S13	68	S12 NOT S9
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Set	Items	Description
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S2	189	AU= REDDIN, ?
S3	114	AU=GRAY-OWEN, ?
S4	3106	AU=BOULTON, ?
S5	3702	S1 OR S2 OR S3 OR S4
S6	196	S5 AND NEISSERIA

S7 198 S5 AND NEISSERIA?
 S8 97 RD S7 (unique items)
 S9 24 S8 AND (OPA OR CEACAM OR BLEB OR VESSICLE)
 S10 0 CEADAM AND OPA AND NEISSERIA?
 S11 368 CEACAM? AND OPA AND NEISSERIA?
 S12 74 RD S11 (unique items)
 S13 68 S12 NOT S9
 ? s s13 not PY>2005

68 S13
 24161939 PY>2005

S14 46 S13 NOT PY>2005

? t s14/7/all

>>>Format 7 is not valid in file 143

14/7/1 (Item 1 from file: 5)
 DIALOG(R)File 5:Biosis Previews(R)
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18720007 BIOSIS NO.: 200600065402

Neisseria gonorrhoeae kills carcinoembryonic antigen-related cellular adhesion molecule 1 (CD66a)-expressing human B cells and inhibits antibody production

AUTHOR: Pantelic Milica; Kim Young-June; Bolland Silvia; Chen Ines; Shively

John; Chen Tie (Reprint)

AUTHOR ADDRESS: Indiana Univ, Sch Med, Div Infect Dis, Dept Microbiol and

Immunol, Walther Oncol Ctr, MS415E, 635 Barnhill Dr, Indianapolis, IN 46202

USA**USA

AUTHOR E-MAIL ADDRESS: tiechen@iupui.edu

JOURNAL: Infection and Immunity 73 (7): p4171-4179 JUL 2005 2005

ISSN: 0019-9567

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Neisseria gonorrhoeae cells (gonococci [GC]), the etiological agents for gonorrhea, can cause repeated infections.

During

and after gonococcal infection, local and systemic antigenococcal antibody levels are low. These clinical data indicate the possibility

that GC may suppress immune responses during infection.

Carcinoembryonic

antigen-related cellular adhesion molecule 1 (CEACAM1 or CD66a), a receptor for GC opacity (Opa) proteins, was shown to mediate inhibitory signals. In the present study, human B cells were activated by

interleukin-2 to express CEACAM1 and then stimulated to secrete antibodies and simultaneously coincubated with Opa(-) and Opal GC of strain MS11. Our results show that this OpaI GC has the ability to

inhibit antibody production. The interaction of GC and CEACAM1 with human peripheral B cells also results in induction of cell death. The same findings were observed in DT40 B cells. This CEACAM1-promoted cell death pathway does not involve the inhibitory signals or the tyrosine phosphatases SHP-1 and SHP-2 but depends on Bruton's tyrosine kinase in DT40 cells. Our results suggest that *Neisseria gonorrhoeae* possesses the ability to suppress antibody production by killing CEACAM1-expressing B cells.

14/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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18600527 BIOSIS NO.: 200510295027

Critical determinants of the interactions of capsule-expressing *Neisseria meningitidis* with host cells: the role of receptor density in increased cellular targeting via the outer membrane Opa proteins

AUTHOR: Bradley Christopher J; Griffiths Natalie J; Rowe Helen A; Heyderman

Robert S; Virji Mumtaz (Reprint)

AUTHOR ADDRESS: Univ Bristol, Sch Med Sci, Dept Pathol and Microbiol, Bristol BS8 1TD, Avon, UK**UK

AUTHOR E-MAIL ADDRESS: m.virji@bristol.ac.uk

JOURNAL: Cellular Microbiology 7 (10): p1490-1503 OCT 2005 2005

ISSN: 1462-5814

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: *Neisseria meningitidis* capsule is an important virulence determinant required for survival in the blood but is reportedly involved in inhibiting cellular interactions mediated by meningococcal outer membrane adhesins. However, evidence from our previous studies suggested that target receptor density on host cells may determine whether or not capsule bacteria can adhere via outer membrane proteins such as Opa. To confirm this and evaluate the impact of capsulation on bacterial interactions, we used Opa(+) and Opa(-) derivatives of capsule and acapsulate meningococcal isolates and transfected cell lines expressing CEACAM1, a receptor targeted by Opa proteins. To assess the extent and rate of cell association, subpopulations of stably transfected Chinese hamster ovary cells with different receptor levels were derived. A quantitative correlation of

CEACAM1 levels and Opa-dependent binding of both capsulate and acapsulate bacteria was demonstrated, which was accelerated at high receptor densities. However, it appears that invasion by Opa(+) capsulate bacteria only occurs when a threshold level of CEACAM density has been reached. Target cells expressing high levels of CEACAM1 (MFI c. 400) bound threefold more, but internalized 20-fold more Opa(+) capsulate bacteria than those with intermediate expression (MFI c. 100). No overall selection of acapsulate phenotype was observed in the internalized population. These observations confirm that capsule may not be an adequate barrier for cellular interactions and demonstrate the role of a host factor that may determine capsulate bacterial invasion potential. Upregulation of CEACAMs, which can occur in response to inflammatory cytokines, could lead to translocation of a small number of fully capsulate bacteria across mucosal epithelium into the bloodstream sufficient to cause a rapid onset of disseminated disease. Thus the data also suggest a novel rationale for the epidemiological observations that individuals with prior infectious/inflammatory conditions carry a high risk of invasive meningococcal disease.

14/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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18386637 BIOSIS NO.: 200510081137
CEACAM1-specific Opa proteins suppress dendritic cell maturation in response to Neisseria gonorrhoeae: Implications for gonorrhea and HIV
AUTHOR: Yu Q (Reprint); Chow E; Yue E; Kovacs C; Dimayuga R; Loutfy M; Ostrowski M; Gray-Owen S D
AUTHOR ADDRESS: Univ Toronto, Div Clin Sci, Toronto, ON M5S 1A8, Canada**
Canada
JOURNAL: Journal of Leukocyte Biology (Suppl. S): p51 04 2004
CONFERENCE/MEETING: 37th Annual Meeting of the Society-for-Leukocyte-Biology Toronto, CANADA October 21 -23, 2004; 20041021
SPONSOR: Soc Leukocyte Biol
ISSN: 0741-5400
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

14/7/4 (Item 4 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)
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18386621 BIOSIS NO.: 200510081121
Bacterial-induced immunosuppression: Neisserial opa proteins
suppress CD4(+) T cell activation via binding to CEACAM1
AUTHOR: Wong H (Reprint); Lee H S W; Boulton I C; Gray-Owen S D
AUTHOR ADDRESS: Univ Toronto, Toronto, ON, Canada**Canada
JOURNAL: Journal of Leukocyte Biology (Suppl. S): p47 04 2004
CONFERENCE/MEETING: 37th Annual Meeting of the
Society-for-Leukocyte-Biology Toronto, CANADA October 21 -23, 2004;
20041021
SPONSOR: Soc Leukocyte Biol
ISSN: 0741-5400
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

14/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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18214958 BIOSIS NO.: 200500122023
CEACAM1-specific Opa proteins suppress dendritic cell
maturation in response to Neisseria gonorrhoeae: Implications for
gonorrhea and HIV
AUTHOR: Yu Q (Reprint); Chow E; Yue E; Kovacs C; Dimayuga R; Loutfy M;
Ostrowski. M; Gray-Owen S D
AUTHOR ADDRESS: Div Clin Sci, Univ Toronto, Toronto, ON, M5S 1A8,
Canada**
Canada
JOURNAL: Journal of Leukocyte Biology Supplement (2004): p51 2004 2004
MEDIUM: print
CONFERENCE/MEETING: 37th Annual Meeting of the Society for Leukocyte
Biology "Host Response to Pathogens" Toronto, ON, Canada October
21-23,
2004; 20041021
SPONSOR: Society for Leukocyte Biology
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

14/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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18214952 BIOSIS NO.: 200500122017
Characterizing neisserial-induced uptake and signaling via the
neutrophil-restricted CEACAM3 receptor
AUTHOR: Sarantis H (Reprint); McCaw S E; Gray-Owen S D

AUTHOR ADDRESS: Univ Toronto, Toronto, ON, Canada**Canada
JOURNAL: Journal of Leukocyte Biology Supplement (2004): p49 2004 2004
MEDIUM: print
CONFERENCE/MEETING: 37th Annual Meeting of the Society for Leukocyte
Biology "Host Response to Pathogens" Toronto, ON, Canada October
21-23,
2004; 20041021
SPONSOR: Society for Leukocyte Biology
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

14/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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18129434 BIOSIS NO.: 200500036499
Retinoic acid treated HL60 cells express CEACAM1 (CD66a) and
phagocytose Neisseria gonorrhoeae
AUTHOR: Pantelic Milica; Chen Ines; Parker James; Zhang Pei; Grunert
Fritz;
Chen Tie (Reprint)
AUTHOR ADDRESS: Sch MedWalther Oncol CtrDiv Infect Dis,Dept Microbiol
and
Immunol, Indiana Univ, Indianapolis, IN, USA**USA
AUTHOR E-MAIL ADDRESS: tiechen@iupui.edu
JOURNAL: FEMS Immunology and Medical Microbiology 42 (2): p261-266
October
1, 2004 2004
MEDIUM: print
ISSN: 0928-8244 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Neisseria gonorrhoeae (gonococci, GC) are phagocytosed by
neutrophils through the interaction between opacity proteins (Opa)
and the CEA (CD66) family of antigens. In order to study this
interaction, we used the human myeloid leukemia HL60 cell line,
which
differentiates into granulocyte-like cells upon treatment with
dimethylsulfoxide (DMSO) or retinoic acid (RA). We found that RA-,
but
not DMSO- or untreated-FIL60 cells, can phagocytose Opal-expressing
gonococci as well as Escherichia coli. The interaction of Opal E.
coli
with RA-treated HL60 cells was inhibited by antibodies against
CEACAM1 Phagocytosis of Opal E. coli was found to be a result of
the expression of CEACAM1 in RA-treated HL60 cells. Our results
indicate that the level of expression of CEACAM1 in HL60 cells can
be regulated by treatment with RA in a differentiation-dependent
manner,

and that this is important for phagocytosis of Opal-expressing gonococci or E. coli. Copyright 2004 Federation of European Microbiological Societies. Published by Elsevier B.V. All rights reserved.

14/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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18126323 BIOSIS NO.: 200500033388
Intranasal immunisation of mice with liposomes containing recombinant meningococcal OpaB and OpaJ proteins
AUTHOR: de Jonge Marien I; Hamstra Hendrik Jan; Jiskoot Wim; Roholl Paul;
Williams Neil A; Dankert Jacob; van Alphen Lock; van der Ley Peter (Reprint)
AUTHOR ADDRESS: Lab Vaccine Res, NVI, POB 457, NL-3720 AL, Bilthoven, Netherlands**Netherlands
AUTHOR E-MAIL ADDRESS: peter.van.der.ley@nvi-vaccin.nl
JOURNAL: Vaccine 22 (29-30): p4021-4028 September 28, 2004 2004
MEDIUM: print
ISSN: 0264-410X _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The opacity (Opa) proteins of Neisseria meningitidis are outer membrane proteins involved in adhesion and invasion of host epithelial cells and are therefore expected to play an important role in colonisation of the nasopharynx. The majority of meningococcal Opa proteins bind to members of the CEACAM receptor family, such as CEA. Blocking of the Opa-CEACAM interaction by mucosal anti-Opa antibodies could thus constitute an important protective mechanism for novel meningococcal vaccines. In this study we analysed the specific anti-Opa antibody responses after intranasal immunisation of mice with liposomes containing purified and native OpaB (recognising the CEA receptor) and OpaJ (no affinity for CEA) proteins. These antigens were combined with or without one of three different adjuvants, i.e. purified meningococcal LPS, monophosphoryl lipid A (MPL) or the B-subunit of Escherichia coli heat-labile enterotoxin (EtxB). After intranasal immunisation with any of these formulations, anti-Opa IgA antibodies were found in nasal lavages and in some cases anti-Opa IgA and IgG antibodies were also found in lung lavages. With OpaJ but not OpaB, significant bactericidal serum titres were obtained. Of the

different adjuvants used, meningococcal LPS gave the strongest overall immune response. Non-adjuvanted liposomal Opa formulations were poorly immunogenic. No differences were found between the immune response in transgenic mice expressing the CEA-receptor and non-transgenic mice, showing that the CEA-Opa interaction does not influence the antibody response. Copyright 2004 Elsevier Ltd. All rights reserved.

14/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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17967675 BIOSIS NO.: 200400338464
Engulfment of *Neisseria gonorrhoeae*: Revealing distinct processes of bacterial entry by individual carcinoembryonic antigen-related cellular adhesion molecule family receptors
AUTHOR: McCaw Shannon E; Liao Edward H; Gray-Owen Scott D (Reprint)
AUTHOR ADDRESS: Dept Med Genet and Microbiol, Univ Toronto, 4381 Med Sci Bldg, 1 Kings Coll Circle, Toronto, ON, M5S 1A8, Canada**Canada
AUTHOR E-MAIL ADDRESS: scott.gray.owen@utoronto.ca
JOURNAL: Infection and Immunity 72 (5): p2742-2752 May 2004 2004
MEDIUM: print
ISSN: 0019-9567 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Individual *Neisseria gonorrhoeae* colony opacity-associated (Opa) protein variants can bind up to four different carcinoembryonic antigen-related cellular adhesion molecule (CEACAM) receptors. Most human cells encountered by gonococci express a combination of CEACAM receptors, thereby complicating the elucidation of intracellular signaling pathways triggered by individual receptors. Here, we compare the process of bacterial engulfment by a panel of stably transfected HeLa epithelial cell lines expressing each CEACAM receptor in isolation. CEACAM1 and CEACAM3 each contain proteinaceous transmembrane and cytoplasmic domains; however, the processes of neisserial uptake mediated by these receptors differ with respect to their susceptibilities to both tyrosine kinase inhibitors and the actin microfilament-disrupting agent cytochalasin D. Neisserial uptake mediated by glycosylphosphatidylinositol (GPI)-anchored CEACAM5 and CEACAM6 was not significantly affected by any of a broad spectrum of inhibitors tested. However,

cleavage of the GPI anchor by phosphatidylinositol-specific phospholipase
C reduced bacterial uptake by HeLa cells expressing CEACAM5, consistent with a single zipper-like mechanism of uptake mediated by this
receptor. Regardless of the CEACAM receptor expressed, internalized gonococci were effectively killed by a microtubule-dependent process that
required acidification of the bacterium-containing phagosome. Given the
phase-variable nature of neisserial Opa proteins, these results indicate that the mechanism of bacterial engulfment and the cellular response to gonococcal infection depend on both the
receptor
specificities of the neisserial Opa protein variants expressed and the spectrum of CEACAM receptors present on target cells, each of which determines the combination of receptors ultimately
engaged.

14/7/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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17594464 BIOSIS NO.: 200300550895
Mapping the binding domains on meningococcal Opa proteins for
CEACAM1 and CEA receptors.
AUTHOR: de Jonge Marien I; Jan Hamstra Hendrik; van Alphen Loek; Dankert
Jacob; van der Ley Peter (Reprint)
AUTHOR ADDRESS: Laboratory of Vaccine Research, Netherlands Vaccine
Institute (NVI), Bilthoven, Netherlands**Netherlands
AUTHOR E-MAIL ADDRESS: Peter.van.der.Ley@nvi-vaccin.nl
JOURNAL: Molecular Microbiology 50 (3): p1005-1015 November 2003 2003
MEDIUM: print
ISSN: 0950-382X _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The opacity (Opa) proteins of pathogenic Neisseria spp. are adhesins, which play an important role in adhesion and invasion
of host cells. Most members of this highly variable family of outer membrane proteins can bind to the human carcinoembryonic antigen-related
cell adhesion molecules (CEACAMs). Several studies have identified the Opa-binding region on the CEACAM receptors; however, not much is known about the binding sites on the Opa proteins for the corresponding CEACAM-receptors. The high degree of sequence variation in the surface-exposed loops of Opa proteins raises the

question how the binding sites for the CEACAM receptors are conserved. *Neisseria meningitidis* strain H44/76 possesses four different Opa proteins, of which OpaA and OpaJ bind to CEACAM1, while OpaB and OpaD bind to CEACAM1 and CEA. A sequence motif involved in binding to CEACAM1 was identified by alanine scanning mutagenesis of those amino acid residues conserved within the hypervariable (HV) regions of all four Opa proteins. Hybrid Opa variants with different combinations of HV-1 and HV-2 derived from OpaB and OpaJ showed a reduced binding to CEACAM1 and CEA, indicating that particular combinations of HV-1 and HV-2 are required for the Opa binding capacity. Homologue scanning mutagenesis was used to generate more refined hybrids containing novel combinations of OpaB and OpaJ sequences within HV-1 and HV-2. They could be used to identify residues determining the specificity for CEA binding. The combined results obtained with mutants and hybrids strongly suggest the existence of a conserved binding site for CEACAM receptors by the interaction of HV-1 and HV-2 regions.

14/7/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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17431651 BIOSIS NO.: 200300390081
Immunoreceptor tyrosine-based activation motif phosphorylation during engulfment of *Neisseria gonorrhoeae* by the neutrophil-restricted CEACAM3 (CD66d) receptor.
AUTHOR: McCaw Shannon E; Schneider Jutta; Liao Edward H; Zimmermann Wolfgang; Gray-Owen Scott D (Reprint)
AUTHOR ADDRESS: Department of Medical Genetics and Microbiology, University of Toronto, Toronto, ON, Canada**Canada
AUTHOR E-MAIL ADDRESS: scott.gray.owen@utoronto.ca
JOURNAL: Molecular Microbiology 49 (3): p623-637 August 2003 2003
MEDIUM: print
ISSN: 0950-382X (ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Gonorrhea is characterized by a purulent urethral or cervical discharge consisting primarily of neutrophils associated with *Neisseria gonorrhoeae*. These interactions are facilitated by gonococcal colony opacity-associated (Opa) protein binding to host cellular CEACAM receptors. Of these, CEACAM3 is restricted to neutrophils and contains an immunoreceptor tyrosine-based activation motif (ITAM) reminiscent of that found within certain phagocytic Fc

receptors. CEACAM3 was tyrosine phosphorylated by a Src family kinase-dependent process upon infection by gonococci expressing CEACAM-specific Opa proteins. This phosphorylation was necessary for efficient bacterial uptake; however, a less efficient uptake process became evident when kinase inhibitors or mutagenesis of the ITAM were used to prevent phosphorylation. Ligated CEACAM3 was recruited to a cytoskeleton-containing fraction, intense foci of polymerized actin were evident where bacteria attached to HeLa-CEACAM3, and disruption of polymerized actin by cytochalasin D blocked all bacterial uptake by these cells. These data support a model whereby CEACAM3 can mediate the Opa-dependent uptake of *N. gonorrhoeae* via either an efficient, ITAM phosphorylation-dependent process that resembles phagocytosis or a less efficient, tyrosine phosphorylation-independent mechanism.

14/7/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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17350072 BIOSIS NO.: 200300307561
Functional activity of antibodies against the recombinant OpaJ protein from *Neisseria meningitidis*.
AUTHOR: de Jonge M I (Reprint); Vidarsson G; van Dijken H H; Hoogerhout P;
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JOURNAL: Infection and Immunity 71 (5): p2331-2340 May 2003 2003
MEDIUM: print
ISSN: 0019-9567 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The opacity proteins belong to the major outer membrane proteins of the pathogenic *Neisseria* and are involved in adhesion and invasion. We studied the functional activity of antibodies raised against the OpaJ protein from strain H44/76. Recombinant OpaJ protein was obtained from *Escherichia coli* in two different ways: cytoplasmic expression in the form of inclusion bodies followed by purification and refolding and cell surface expression followed by isolation of outer membrane complexes (OMCs). Immunization with purified protein and Quillaja saponin A (QuilA) induced high levels of Opa-specific

antibodies, whereas the E. coli OMC preparations generally induced lower levels of antibodies. Two chimeric Opa proteins, hybrids between OpaB and OpaJ, were generated to demonstrate that the hypervariable region 2 is immunodominant. Denatured OpaJ with QuilA induced high levels of immunoglobulin G2a (IgG2a) in addition to IgG1, whereas refolded OpaJ with QuilA induced IgG1 exclusively. These sera did not induce significant complement-mediated killing. However, all sera blocked the interaction of OpaJ-expressing bacteria to CEACAM1-transfected cells. In addition, cross-reactive blocking of OpaB-expressing bacteria to both CEACAM1- and CEA-transfected cells was found for all sera. Sera raised against purified OpaJ and against OpaJ-containing meningococcal OMCs also blocked the nonopsonic interaction of Opa-expressing meningococci with human polymorphonuclear leukocytes.

14/7/13 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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17296694 BIOSIS NO.: 200300255413
Phosphatidylinositol 3-kinases in carcinoembryonic antigen-related cellular adhesion molecule-mediated internalization of Neisseria gonorrhoeae.
AUTHOR: Booth James W; Telio David; Liao Edward H; McCaw Shannon E; Matsuo Tsuyoshi; Grinstein Sergio; Gray-Owen Scott D (Reprint)
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JOURNAL: Journal of Biological Chemistry 278 (16): p14037-14045
April 18, 2003 2003
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Neisseria gonorrhoeae can be internalized by mammalian cells through interactions between bacterial opacity-associated (Opa) adhesins and members of the human carcinoembryonic antigen-related cellular adhesion molecule (CEACAM) family. We examined the role of phosphatidylinositol 3-kinases (PI3Ks) in gonococcal

invasion of epithelial cell lines expressing either CEACAM1 or CEACAM3. CEACAM3-mediated internalization, but not that mediated by CEACAM1, was accompanied by localized and transient accumulation of the class I PI3K product phosphatidylinositol 3,4,5-trisphosphate at sites of bacterial engulfment. Inhibition of phosphatidylinositol 3-kinases reduced CEACAM3-mediated uptake but, paradoxically, led to an increase in intracellular survival of bacteria internalized via either CEACAM1 or CEACAM3, suggesting additional roles for PI3K products. Consistent with this finding, the class III PI3K product phosphatidylinositol 3-phosphate accumulated and persisted in the membrane of gonococcal phagosomes after internalization. Inhibition of PI3K blocked phagosomal acquisition of the late endosomal marker lysosome-associated membrane protein 2 and reduced phagosomal acidification. Inhibiting phagosomal acidification with concanamycin A also increased survival of intracellular gonococci. These results suggest two modes of action of phosphatidylinositol 3-kinases during internalization of gonococci: synthesis of phosphatidylinositol 3,4,5-trisphosphate is important for CEACAM3-mediated uptake, while phosphatidylinositol 3-phosphate is needed for phagosomal maturation and acidification, which are required for optimal bacterial killing.

14/7/14 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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17099011 BIOSIS NO.: 200300057730
Neisserial binding to CEACAM1 arrests the activation and proliferation of CD+ T lymphocytes.
AUTHOR: Boulton Ian C; Gray-Owen Scott D (Reprint)
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JOURNAL: Nature Immunology 3 (3): p229-236 March 2002 2002
MEDIUM: print
ISSN: 1529-2908 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Infection with Neisseria gonorrhoeae can trigger an intense

inflammatory response, yet there is little specific immune response or development of immune memory. In addition, gonorrhea typically correlates with a transient reduction in T lymphocyte counts in blood, and these populations recover when gonococcal infection is resolved. Such observations suggest that the gonococci have a suppressive effect on the host immune response. We report here that *N. gonorrhoeae* Opa proteins were able to bind CEACAM1 expressed by primary CD4+ T lymphocytes and suppress their activation and proliferation. CEACAM1 bound by gonococcal Opa52 associated with the tyrosine phosphatases SHP-1 and SHP-2, which implicates the receptor's ITIM (immunoreceptor tyrosine-based inhibitory motif) in this effect.

14/7/15 (Item 15 from file: 5)
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17064534 BIOSIS NO.: 200300023253
Conformational analysis of opacity proteins from *Neisseria meningitidis*.

AUTHOR: de Jonge Marien I (Reprint); Bos Martine P; Hamstra Hendrik J;
Jiskoot Wim; van Ulsen Peter; Tommassen Jan; van Alphen Loek; van der Ley
Peter

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Netherlands

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JOURNAL: European Journal of Biochemistry 269 (21): p5215-5223
November
2002 2002

MEDIUM: print
ISSN: 0014-2956 (ISSN print)
DOCUMENT TYPE: Article
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LANGUAGE: English

ABSTRACT: Opacity-associated (Opa) proteins are outer membrane proteins which play a critical role in the adhesion of pathogenic *Neisseria* spp. to epithelial and endothelial cells and polymorphonuclear neutrophils. The adherence is mainly mediated by the CD66-epitope-containing members of the carcinoembryonic-antigen family of human cell-adhesion molecules (CEACAM). For the analysis of the specific interactions of individual Opa proteins with their receptors, pure protein is needed in its native conformation. In this

study, we describe the isolation and structural analysis of opacity proteins OpaJ129 and OpaB128 derived from *Neisseria meningitidis* strain H44/76. When the Opa proteins were produced with the phoE signal sequence in *Escherichia coli*, they were localized at the cell surface and the recombinant bacteria were found to specifically interact with CEACAM1. For refolding and purification, the proteins were overproduced without their signal sequences in *E. coli*, resulting in its cytoplasmic accumulation in the form of inclusion bodies. After solubilization of the inclusion bodies in urea, the proteins could be folded efficiently in vitro, under alkaline conditions by dilution in ethanolamine and the detergent n-dodecyl-N,N-dimethyl-1-ammonio-3-propane-sulfonate (SB12). The structure of the refolded and purified proteins, determined by circular dichroism, indicated a high content of beta-sheet conformation, which is consistent with previously proposed topology models for Opa proteins. A clear difference was found between the binding of refolded vs. denatured OpaJ protein to the N-A1 domain of CEACAM1. Almost no binding was found with the denatured Opa protein, showing that the Opa-receptor interaction is conformation-dependent.

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16655836 BIOSIS NO.: 200200249347
Carcinoembryonic antigen family receptor recognition by gonococcal Opa proteins requires distinct combinations of hypervariable Opa protein domains
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JOURNAL: Infection and Immunity 70 (4): p1715-1723 April, 2002 2002
MEDIUM: print
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: *Neisseria* Opa proteins function as a family of adhesins that bind heparan sulfate proteoglycan (HSPG) or carcinoembryonic antigen family (CEACAM) receptors on human host cells. In order to define the CEACAM binding domain on Opa

proteins, we tested the binding properties of a series of gonococcal (strain MS11) recombinants producing mutant and chimeric Opa proteins with alterations in one or more of the four surface-exposed loops. Mutagenesis demonstrated that the semivariable domain, present in the first loop, was completely dispensable for CEACAM binding. In contrast, the two hypervariable (HV) regions present in the second and third loops were essential for binding; deletion of either domain resulted in loss of receptor recognition. Deletion of the fourth loop resulted in a severe decrease in Opa expression at the cell surface and could therefore not be tested for CEACAM binding. Chimeric Opa variants, containing combinations of HV regions derived from different CEACAM binding Opa proteins, lost most of their receptor binding activity. Some chimeric variants gained HSPG binding activity. Together, our results indicate that full recognition of CEACAM receptors by Opa proteins requires a highly coordinate interplay between both HV regions. Furthermore, shuffling of HV regions may result in novel HSPG receptor binding activity.

14/7/17 (Item 17 from file: 5)
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16624189 BIOSIS NO.: 200200217700
Nuclear factor-kappaB directs carcinoembryonic antigen-related cellular adhesion molecule 1 receptor expression in Neisseria gonorrhoeae-infected epithelial cells
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JOURNAL: Journal of Biological Chemistry 277 (9): p7438-7446 March 1, 2002
2002
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The human-specific pathogen Neisseria gonorrhoeae expresses opacity-associated (Opa) protein adhesins that bind to various members of the carcinoembryonic antigen-related cellular adhesion

molecule (CEACAM) family. In this study, we have analyzed the mechanism underlying *N. gonorrhoeae*-induced CEACAM up-regulation in epithelial cells. Epithelial cells represent the first barrier for the microbial pathogen. We therefore characterized CEACAM expression in primary human ovarian surface epithelial (HOSE) cells and found that CEACAM1-3 (L, S) and CEACAM1-4 (L, S) splice variants mediate an increased Opa52-dependent gonococcal binding to HOSE cells. Up-regulation of these CEACAM molecules in HOSE cells is a direct process that takes place within 2 h postinfection and depends on close contact between microbial pathogen and HOSE cells. *N. gonorrhoeae*-triggered CEACAM1 up-regulation involves activation of the transcription factor nuclear factor kappaB (NF-kappaB), which translocates as a p50/p65 heterodimer into the nucleus, and an NF-kappaB-specific inhibitory peptide inhibited CEACAM1-receptor up-regulation in *N. gonorrhoeae*-infected HOSE cells. Bacterial lipopolysaccharides did not induce NF-kappaB and CEACAM up-regulation, which corresponds to our findings that HOSE cells do not express toll-like receptor 4. The ability of *N. gonorrhoeae* to up-regulate its epithelial receptor CEACAM1 through NF-kappaB suggests an important mechanism allowing efficient bacterial colonization during the initial infection process.

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16614605 BIOSIS NO.: 200200208116

Distinct mechanisms of internalization of *Neisseria gonorrhoeae* by members of the CEACAM receptor family involving Rac1- and Cdc42-dependent and -independent pathways

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JOURNAL: EMBO (European Molecular Biology Organization) Journal 21 (4): p

560-571 February 15, 2002 2002

MEDIUM: print

ISSN: 0261-4189

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Opa adhesins of pathogenic *Neisseria* species target

four members of the human carcinoembryonic antigen-related cellular adhesion molecule (CEACAM) family. CEACAM receptors mediate opsonization-independent phagocytosis of *Neisseria gonorrhoeae* by human granulocytes and each receptor individually can mediate gonococcal

invasion of epithelial cells. We show here that gonococcal internalization occurs by distinct mechanisms depending on the CEACAM receptor expressed. For the invasion of epithelial cell lines via CEACAM1 and CEACAM6, a pathogen-directed reorganization of the actin cytoskeleton is not required. In marked contrast, ligation of CEACAM3 triggers a dramatic but localized reorganization of the host cell surface leading to highly efficient engulfment of bacteria in a process regulated by the small GTPases

Rac1

and Cdc42, but not Rho. Two tyrosine residues of a cytoplasmic immune

receptor tyrosine-based activating motif of CEACAM3 are essential for the induction of phagocytic actin structures and subsequent gonococcal internalization. The granulocyte-specific CEACAM3 receptor has properties of a single chain phagocytic receptor and

may

thus contribute to innate immunity by the elimination of *Neisseria* and other CEACAM-binding pathogens that colonize human mucosal surfaces.

14/7/19 (Item 19 from file: 5)

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16607957 BIOSIS NO.: 200200201468

The Opacity (Opa) proteins of *Neisseria gonorrhoeae* strain

FA1090 bind heparan sulfate proteoglycan (HSPG) and Carcinoembryonic Antigen (CEACAM) receptors

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JOURNAL: Abstracts of the General Meeting of the American Society for Microbiology 101 p303-304 2001 2001

MEDIUM: print

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LANGUAGE: English

ABSTRACT: *Neisseria gonorrhoeae*, which causes the sexually transmitted disease gonorrhea, is a pathogen that only infects humans.

The interaction of *N. gonorrhoeae* with host tissues is mediated by several bacterial surface components, including the Opacity (Opa) proteins. A gonococcal strain can express up to 12 unique Opa protein variants and the sequence of these variants differs from strain to strain. The antigenic variability of Opa proteins is due to the presence of a semi-variable (SV) and two hypervariable (HV1 and HV2) regions that punctuate the conserved portion of Opa sequence. Opa proteins from strain MS11 interact with two classes of eukaryotic cell surface receptors: heparan sulfate proteoglycan (HSPG) and members of the Carcinoembryonic Antigen (CEACAM) family. To understand the relationship between Opa sequence and receptor recognition, we evaluated the receptor binding properties of Opa proteins from strain FA1090, the only other strain for which the sequence of the entire opa gene repertoire is known. We tested a panel of FA1090 variants that singly expressed Opa proteins A-K for binding to heparin, a receptor analog of HSPG, and to recombinant CEACAM1, 3, 6, 8 and CEA proteins. The receptor binding pattern of FA1090 Opa proteins had similarities to that of MS11: Opa variants displayed differential recognition of HSPG and 4 of 5 CEACAM receptors. One Opa protein, OpaI, recognized both classes of receptors, HSPG and CEACAM. In many cases, Opa proteins with identical receptor specificities did not have identical sequence, suggesting that the receptor binding domain is not defined by primary sequence.

Mutational analysis of recombinant OpaB provided further evidence that the receptor binding domain is conformationally dependent. Insertion of a FLAG epitope (7 a.a.) or a conservative 3 a.a. alanine substitution in the surface exposed domains of the protein resulted in the loss of binding to CEACAM1. Our results indicate that receptor specificity is defined by the particular combination of variable regions and involves the physical interaction of multiple regions of the Opa protein.

14/7/20 (Item 20 from file: 5)
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16460908 BIOSIS NO.: 200200054419
 CEACAM1 expression induced by *Neisseria gonorrhoeae*
 AUTHOR: Muenzner-Voigt Petra (Reprint); Meyer Thomas F (Reprint); Hauck Christof R (Reprint)
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 JOURNAL: Biology of the Cell (Paris) 93 (3-4): p212 October, 2001
 2001

MEDIUM: print
CONFERENCE/MEETING: First Joint French-German Congress on Cell
Biology
Strasbourg, France November 07-09, 2001; 20011107
SPONSOR: Societe de Biologie Cellulaire de France
Deutsche Gesellschaft fuer Zellbiologie
ISSN: 0248-4900
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14/7/21 (Item 21 from file: 5)
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16355415 BIOSIS NO.: 200100527254
Identification and comparison of residues critical for cell-adhesion
activities of two neutrophil CD66 antigens, CEACAM6 and
CEACAM8
AUTHOR: Kuroki Motomu (Reprint); Abe Hironori; Imakiirei Takayuki;
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Shaoxi; Uchida Hiroko; Yamauchi Yasushi; Oikawa Shinzo; Kuroki
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JOURNAL: Journal of Leukocyte Biology 70 (4): p543-550 October, 2001
2001
MEDIUM: print
ISSN: 0741-5400
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: CEACAM6 (CD66c) and CEACAM8 (CD66b) are cell-adhesion
proteins on neutrophils that belong to the human carcinoembryonic
antigen
(CEA) family. CEACAM6 reveals homophilic adhesion and heterophilic
adhesion to other CEACAM family antigens including CEACAM8,
CEACAM1, and CEA, whereas CEACAM8 exhibits only heterophilic
adhesion to CEACAM6. Here, we investigated and compared structural
requirements for the homophilic adhesion of CEACAM6 and
heterophilic adhesion between CEACAM6 and CEACAM8 at the
amino acid level by using CHO transfectants expressing their mutant
and
chimeric proteins. The NH2-terminal domain (N-domain) of CEACAM6
expressed on a CHO cell was suggested to bind the N-domain of
CEACAM6 or CEACAM8 on the opposing cell. By
homologue-scanning mutagenesis, we found that the locations of the
sequences critical for the adhesion of CEACAM6 to itself and to

CEACAM8 are overlapped and that they are highly similar but not identical to the locations of the residues previously shown to be essential for the binding of CEACAM antigens to Opa proteins of pathogenic *Neisseriae*. Our findings imply that subtle differences in the N-domain sequences determine the specificity of the CEACAM antigens on neutrophils for interaction with the same or different CEACAM antigens and the bacterial proteins.

14/7/22 (Item 22 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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16279541 BIOSIS NO.: 200100451380
Homophilic adhesion of human CEACAM1 involves N-terminal domain interactions: Structural analysis of the binding site
AUTHOR: Watt Suzanne M (Reprint); Teixeira Ana M; Zhou Guang-Qian; Doyonnas
Regis; Zhang Youyi; Grunert Fritz; Blumberg Richard S; Kuroki Motomu;
Skubitz Keith M; Bates Paul A
AUTHOR ADDRESS: Stem Cell Laboratory, National Blood Service, John Radcliffe Hospital, Headington, Oxford, OX3 9DS, UK**UK
JOURNAL: Blood 98 (5): p1469-1479 September 1, 2001 2001
MEDIUM: print
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: CEACAM1 on leukocytic, endothelial, and epithelial cells functions in homophilic adhesion, tumor suppression, regulating cell adhesion and proliferation, and in heterophilic adhesion as a receptor for E-selectin and *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Haemophilus influenzae*, and murine coronaviruses. The 8 transmembrane isoforms of human CEACAM1 possess an extracellular N-terminal IgV domain, followed by variable numbers of IgC2 domains. To establish which key amino acids contribute specifically to CEACAM1 homophilic adhesion, exposed amino acids in the N-terminal domain of a soluble form of CEACAM1 were subjected to mutagenesis. Analyses of mutant proteins with conformationally dependent antibodies indicated that most mutations did not substantially affect the structural integrity of CEACAM1. Nevertheless, decreased adhesion was observed for the single mutants V39A or D40A (single-letter amino acid codes) in the CC loop and for the triple mutants located in the GFCC'C" face of the

N-terminal domain. Interestingly, whereas single mutations in R64 or D82 that are predicted to form a salt bridge between the base of the D and F beta strands close to the critical V39 and D40 residues also abolish adhesion, an amino acid swap (R64D and D82R), which maintains the salt bridge was without significant effect. These studies indicate that the CC' loop plays a crucial role in the homophilic adhesion of CEACAM1. They further predict that specific hydrophobic amino acid residues on the nonglycosylated GFCC'C" face of CEACAM1 N-terminal domain are not only involved in heterophilic interactions with Opa proteins and H influenzae, but are also critical for protein-protein interactions between 2 CEACAM1 molecules on opposing cells.

14/7/23 (Item 23 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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16211771 BIOSIS NO.: 200100383610
The CGM1a (CEACAM3/CD66d)-mediated phagocytic pathway of *Neisseria gonorrhoeae* expressing opacity proteins is also the pathway to cell death
AUTHOR: Chen Tie (Reprint); Bolland Silvia; Chen Ines; Parker James; Pantelic Milica; Grunert Fritz; Zimmermann Wolfgang
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JOURNAL: Journal of Biological Chemistry 276 (20): p17413-17419 May 18, 2001 2001
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Phagocytosis of Opa+ *Neisseria gonorrhoeae* (gonococcus, GC) by neutrophils is in part dependent on the interaction of Opa proteins with CGM1a (CEACAM3/CD66d) antigens, a neutrophil-specific receptor. However, the signaling pathways leading to phagocytosis have not been characterized. Here we show that interaction of Opa bacteria with neutrophils or CGM1a-transfected DT40 cells induces

calcium flux, which correlates with phagocytosis of bacteria. We identified an immunoreceptor tyrosine-based activation motif (ITAM) in CGM1a, and showed that the ability of CGM1a to transduce signals and mediate phagocytosis was abolished by mutation of the ITAM tyrosines. We also demonstrated that CGM1a-ITAM-mediated bacterial phagocytosis is dependent on Syk and phospholipase C activity in DT40 cells. Unexpectedly, the activation of the CGM1a-ITAM phagocytic pathway by Opa+ GC results in induction of cell death.

14/7/24 (Item 24 from file: 5)
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16200415 BIOSIS NO.: 200100372254
Pathogenic Neisseria trigger expression of their carcinoembryonic antigen-related cellular adhesion molecule 1 (CEACAM1; previously CD66a) receptor on primary endothelial cells by activating the immediate early response transcription factor, nuclear factor-kappaB
AUTHOR: Muenzner Petra; Naumann Michael; Meyer Thomas F (Reprint); Gray-Owen Scott D
AUTHOR ADDRESS: Abteilung Infektionsbiologie, Max-Planck-Institut fuer Biologie, Spemannstrasse 34, 72076, Tuebingen, Germany**Germany
JOURNAL: Journal of Biological Chemistry 276 (26): p24331-24340 June 29, 2001 2001
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Neisseria gonorrhoeae express opacity-associated (Opa) protein adhesions that mediate binding to various members of the carcinoembryonic antigen-related cellular adhesion molecule (CEACAM; previously CD66) receptor family. Although human umbilical vein endothelial cells express little CEACAM receptor in vitro, we found neisserial infection to induce expression of CEACAM1, CEACAM1-3L, and CEACAM1-4L splice variants. This mediates an increased Opa52-dependent binding of gonococci by these cells. The induced receptor expression did not require bacterial Opa expression, but it was more rapid with adherent bacteria. Because the time course of induction was similar to that seen for induced proinflammatory cytokines, we tested whether CEACAM1 expression could be controlled by a similar mechanism. Gonococcal infection activated a nuclear factor-kappaB (NF-kappaB) heterodimer consisting of p50 and p65, and inhibitors that prevent the nuclear translocation of

activated NF-kappaB complex inhibited CEACAM1 transcript expression. Each of these effects could be mimicked by using culture filtrates or purified lipopolysaccharide instead of intact bacteria. Together, our results support a model whereby the outer membrane "blebs"

that are actively released by gonococci trigger a Toll-like receptor-4-dependent activation of NF-kappaB, which up-regulates the expression of CEACAM1 to allow Opa52-mediated neisserial binding. The regulation of CEACAM1 expression by NF-kappaB also implies a broader role for this receptor in the general inflammatory response to infection.

14/7/25 (Item 25 from file: 5)
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15795681 BIOSIS NO.: 200000513994
The identification of critical adhesiotopes on the N-domain of human CEACAM1 required for homophilic interactions
AUTHOR: Watt S M (Reprint); Teixeira A M; Blumberg R; Kuroki M; Skubitz K M
; Bates P A
AUTHOR ADDRESS: MRC Molecular Haematology Unit, Institute of Molecular Medicine, Oxford, Oxfordshire, UK**UK
JOURNAL: Tissue Antigens 55 (Supplement 1): p105 2000 2000
MEDIUM: print
CONFERENCE/MEETING: 7th Workshop and Conference on Human Leucocyte Differentiation Antigens Harrogate, England, UK June 20-24, 2000; 20000620
ISSN: 0001-2815
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14/7/26 (Item 26 from file: 5)
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15720720 BIOSIS NO.: 200000439033
Acid sphingomyelinase is involved in CEACAM receptor-mediated phagocytosis of Neisseria gonorrhoeae
AUTHOR: Hauck C R; Grassme H; Bock J; Jendrosseck V; Ferlinz K; Meyer T F;
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AUTHOR ADDRESS: Department of Physiology, University of Tuebingen, Gmelinstrasse 5, 72076, Tuebingen, Germany**Germany
JOURNAL: FEBS Letters 478 (3): p260-266 4 August, 2000 2000
MEDIUM: print
ISSN: 0014-5793
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The interaction with human phagocytes is a hallmark of symptomatic *Neisseria gonorrhoeae* infections. Gonococcal outer membrane proteins of the Opa family induce the opsonin-independent uptake of the bacteria that relies on CEACAM receptors and an active signaling machinery of the phagocyte. Here, we show that CEACAM receptor-mediated phagocytosis of Opa52-expressing *N. gonorrhoeae* into human cells results in a rapid activation of the acid sphingomyelinase. Inhibition of this enzyme by imipramine or SR33557 abolishes opsonin-independent internalization without affecting bacterial adherence. Reconstitution of ceramide, the product of acid sphingomyelinase activity, in imipramine- or SR33557-treated cells restores internalization of the bacteria. Furthermore, we demonstrate that CEACAM receptor-initiated stimulation of other signalling molecules, in particular Src-like tyrosine kinases and Jun N-terminal kinases, requires acid sphingomyelinase. These studies provide evidence for a crucial role of the acid sphingomyelinase for CEACAM receptor-initiated signalling events and internalization of Opa52-expressing *N. gonorrhoeae* into human neutrophils.

14/7/27 (Item 27 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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15563891 BIOSIS NO.: 200000282204

Carcinoembryonic antigen family receptor specificity of *Neisseria meningitidis* Opa variants influences adherence to and invasion of proinflammatory cytokine-activated endothelial cells
AUTHOR: Muenzner Petra; Dehio Christoph; Fujiwara Taku; Achtman Mark; Meyer

Thomas F (Reprint); Gray-Owen Scott D
AUTHOR ADDRESS: Abteilung Molekulare Biologie, Max-Planck-Institut fuer

Infektionsbiologie, Monbijoustrasse 2, 10117, Berlin, Germany**Germany

JOURNAL: Infection and Immunity 68 (6): p3601-3607 June, 2000 2000

MEDIUM: print

ISSN: 0019-9567

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The carcinoembryonic antigen (CEA) family member CEACAM1 (previously called biliary glycoprotein or CD66a) was previously shown to

function as a receptor that can mediate the binding of Opa protein-expressing *Neisseria meningitidis* to both neutrophils and epithelial cells. Since neutrophils and polarized epithelia have both been shown to coexpress multiple CEACAM receptors, we have now extended this work to characterize the binding specificity of meningococcal Opa proteins with other CEA family members. To do so, we used recombinant *Escherichia coli* expressing nine different Opa variants from three meningococcal strains and stably transfected cell lines expressing single members of the CEACAM family. These infection studies demonstrated that seven of the nine Opa variants bound to at least one CEACAM receptor and that binding to each of these receptors is sufficient to trigger the Opa-dependent bacterial uptake by these cell lines. The other two Opa variants do not appear to bind to either CEACAM receptors or heparan sulfate proteoglycan receptors, which are bound by some gonococcal Opa variants, thus implying a novel class of Opa proteins. We have also extended previous studies by demonstrating induction of CEACAM1 expression after stimulation of human umbilical vein endothelial cells with the proinflammatory cytokine tumor necrosis factor alpha, which is present in high concentrations during meningococcal disease. This induced expression of CEACAM1 leads to an increased Opa-dependent bacterial binding and invasion into the primary endothelia, implying that these interactions may play an important role in the pathogenesis of invasive meningococcal disease.

14/7/28 (Item 1 from file: 6)

DIALOG(R)File 6:NTIS

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2326239 NTIS Accession Number: ADA435969/XAB

Examination of *Neisseria Gonorrhoeae* Opacity Protein Expression During Experimental Murine Genital Tract Infection
(Doctoral thesis)

Simms, A. N.

Uniformed Services University of the Health Sciences, Bethesda, MD.
Hebert (F.

Edward) School of Medicine.

Corp. Source Codes: 081102006; 426710

2005 193p

Languages: English Document Type: Thesis

Journal Announcement: USGRDR0523

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Port Royal Road, Springfield, VA, 22161, USA.

NTIS Prices: PC A10/MF A03

Country of Publication: United States

The opacity (Opa) proteins of *Neisseria gonorrhoeae* are a family of phasevariable outer membrane proteins that bind to host cells.

Phase variable expression occurs via a reversible frameshift mechanism within each opa gene. Opa protein expression is selected for, or induced during experimental genital tract infection of female mice, similar to that which was reported in male volunteers. Using a genetically marked strain of FA1090 to follow recovery of a specific population of Opa variants during murine infection, here we showed that selection of a pre-existing population of Opa-positive gonococci present in the inoculum was responsible for the reisolation of mainly Opa-positive variants early during infection. We conclude that the preferential recovery of Opa -positive gonococci observed early during murine infection is due to selection of a pre-existing population of Opa-positive variants caused by factors other than binding to human CEACAM receptors. In long-term infection of mice, a cyclical pattern of Opa protein expression was observed in which a decreased recovery of Opa-positive variants followed early selection for Opa protein expression; reemergence of Opa-positive gonococci occurred later in infection.

14/7/29 (Item 1 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
(c) 2009 CSA. All rts. reserv.

0002126178 IP ACCESSION NO: 4745126
The structural basis of CEACAM-receptor targeting by neisserial Opa proteins: Response

Virji, M
Dept of Pathology and Microbiology, University of Bristol, Medical Sciences
Building, University Walk, Bristol, UK BS8 1TD

Trends in Microbiology, v 8, n 6, p 260-261, June 2000
PUBLICATION DATE: 2000

DOCUMENT TYPE: Journal Article; Review
RECORD TYPE: Abstract
LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0966-842X

DOI: 10.1016/S0966-842X(00)01772-8

FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

ABSTRACT:

Billker et al. have written a lucid and up-to-date article on the interactions of pathogenic neisserial colony opacity-associated (Opa) proteins with carcinoembryonic-antigen-related cellular adhesion molecules (CEACAMs). I would like to add a few supplementary comments, some of which pertain to Opa proteins in a wider context, taking into account other species within the genus *Neisseria*.

14/7/30 (Item 1 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

(c) 2009 The Thomson Corp. All rts. reserv.

14310709 Genuine Article#: 959IB Number of References: 54

Title: CEACAM engagement by human pathogens enhances cell adhesion and counteracts bacteria-induced detachment of epithelial cells

Author(s): Muenzner P; Rohde M; Kneitz S; Hauck CR (REPRINT)

Corporate Source: Univ Wurzburg, Zentrum Infect Forsch, D-97070

Wurzburg//Germany/ (REPRINT); Univ Wurzburg, Zentrum Infect

Forsch, D-97070 Wurzburg//Germany/; Gesell Biotechnol Forsch

mbH, D-38124

Braunschweig//Germany/; Univ Wurzburg, Inst Klin Biochem &

Pathobiochem, D-97078 Wurzburg//Germany/(

christof.hauck@mail.uni-wuerzburg.de)

Journal: JOURNAL OF CELL BIOLOGY, 2005, V170, N5 (AUG 29), P825-836

ISSN: 0021-9525 Publication date: 20050829

Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY

10021 USA

Language: English Document Type: ARTICLE

Abstract: Exfoliation, which is the detachment of infected epithelial cells, is an innate defense mechanism to prevent bacterial colonization. Indeed, infection with *Neisseria gonorrhoeae* induced epithelial detachment from an extracellular matrix (ECM) substrate in vitro. Surprisingly, variants of *N. gonorrhoeae* that bind

to human carcinoembryonic antigen-related cell adhesion molecules

(CEACAMs) failed to induce detachment and, instead, promoted enhanced host cell adhesion to the ECM. Microarray analysis revealed

that CEACAM engagement by several human pathogens triggers expression of CD105. Blockage of CD105 expression by antisense oligonucleotides abolished infection-induced cell adhesion. The expression of full-length CD105 promoted cell adhesion to the ECM

and

was sufficient to prevent infection-induced detachment. The

CD105-mediated increase in cell adhesion was dependent on the presence and function of integrin beta 1. CD105 expression did not elevate cellular integrin levels but caused a dramatic increase in the ECM-binding capacity of the cells, suggesting that CD105 affects integrin activity. The exploitation of CEACAMs to trigger CD105 expression and to counteract infection-induced cell detachment represents an intriguing adaptation of pathogens that are specialized to colonize the human mucosa.

14/7/31 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

13623275 Genuine Article#: 89800 Number of References: 58
Title: Carcinoembryonic antigen-related cell adhesion molecule (CEACAM)-binding recombinant polypeptide confers protection against infection by respiratory and urogenital pathogens
Author(s): Hill DJ; Edwards AM; Rowe HA; Virji M (REPRINT)
Corporate Source: Univ Bristol, Dept Pathol & Microbiol, Bristol BS8 1TD/Avon/England/ (REPRINT); Univ Bristol, Dept Pathol & Microbiol, Bristol BS8 1TD/Avon/England/; Univ Minnesota, Dept Oral Sci, Minneapolis//MN/55455 (m.virji@bristol.ac.uk)
Journal: MOLECULAR MICROBIOLOGY, 2005, V55, N5 (MAR), P1515-1527
ISSN: 0950-382X Publication date: 20050300
Publisher: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4 2DG,
OXON, ENGLAND
Language: English Document Type: ARTICLE
Abstract: The human-specific pathogens *Neisseria meningitidis*, *N. gonorrhoea*, *Haemophilus influenzae* and *Moraxella catarrhalis* share the property of targeting the carcinoembryonic antigen (CEA)-related cell adhesion molecules (CEACAMs) expressed on human epithelia. CEACAMs are signalling receptors implicated in cell adhesion and regulation of several physiological functions. Their targeting by pathogens can lead to tissue invasion. Although the CEACAM-binding ligands of the bacteria are structurally diverse, they target a common site on the receptor. We have generated a recombinant polypeptide that blocks the interactions of the mucosal pathogens with human epithelial cells and antibodies against it inhibit *M. catarrhalis* interactions with the receptor. As such, it is a potential antimicrobial agent to prevent infection via a strategy unlikely to promote bacterial resistance and a vaccine candidate against *M. catarrhalis*. In addition, it could serve more widely as a novel

research tool and as a potential therapeutic agent in CEACAM
-based physiological disorders.

14/7/32 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

12753244 Genuine Article#: 818FQ Number of References: 95
Title: Differential recognition of members of the carcinoembryonic
antigen

family by Afa/Dr adhesins of diffusely adhering *Escherichia coli*
(Afa/Dr DAEC)

Author(s): Berger CN; Billker O; Meyer TF; Servin AL (REPRINT) ;
Kansau I
Corporate Source: Univ Paris 11, Fac Pharm, INSERM, U510, F-92296
Chatenay

Malabry//France/ (REPRINT); Univ Paris 11, Fac Pharm, INSERM,
U510, F-92296 Chatenay Malabry//France/; Max Planck Inst Infekt
Biol, Mol

Biol Abt, D-10117 Berlin//Germany/; Univ London Imperial Coll Sci
Technol & Med, Dept Biol Sci, London SW7 2AZ//England/

Journal: MOLECULAR MICROBIOLOGY, 2004, V52, N4 (MAY), P963-983

ISSN: 0950-382X Publication date: 20040500

Publisher: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4
2DG,

OXON, ENGLAND

Language: English Document Type: ARTICLE

Abstract: Little is known about the molecular bases underlying the
virulence of diffusely adhering *Escherichia coli* (DAEC)
harbouring the

Afa/Dr family of adhesins. These adhesins recognize as receptors
the

GPI-anchored proteins CD55 (decay-accelerating factor, DAF) and
CD66e

(carcinoembryonic antigen, CEA). CD66e is a member of the
CEA-related

cell adhesion molecules (CEACAM) family, comprising seven
members. We analysed the interactions of Afa/Dr DAEC with the
CEACAMs using CEACAM-expressing CHO and HeLa cells. The
results demonstrate that only *E. coli* expressing a subfamily of

Afa/Dr
adhesins, named here Afa/Dr-I, including Dr, F1845 and AfaE-III
adhesins, bound onto CHO cells expressing CEACAM1, CEA or
CEACAM6. Whereas all the Afa/Dr adhesins elicit recruitment of
CD55 around adhering bacteria, only the Afa/Dr-I subfamily
elicits the

recruitment of CEACAM1, CEA and CEACAM6. In addition,
although CEACAM3 is not recognized as a receptor by the subfamily
of Afa/Dr adhesins, it is recruited around bacteria in HeLa
cells. The

recruited CEACAM1, CEA and CEACAM6 around adhering bacteria

resist totally or in part a detergent extraction, whereas the recruited CEACAM3 does not. Finally, the results show that recognition of CEA and CEACAM6, but not CEACAM1, is accompanied by tight attachment to bacteria of cell surface microvilli-like extensions, which are elongated. Moreover, recognition of CEA is accompanied by an activation of the Rho GTPase Cdc42 and by a phosphorylation of ERM, which in turn elicit the observed cell surface microvilli-like extensions.

14/7/33 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

12396734 Genuine Article#: 763GC Number of References: 45
Title: Granulocyte CEACAM3 is a phagocytic receptor of the innate immune system that mediates recognition and elimination of human-specific pathogens
Author(s): Schmitter T; Agerer F; Peterson L; Munzner P; Hauck CR (REPRINT)
Corporate Source: Univ Wurzburg, Zentrum Infekt Forsch, Röntgenring 11/D-97070 Wurzburg//Germany/ (REPRINT); Univ Wurzburg, Zentrum Infekt Forsch, D-97070 Wurzburg//Germany/
Journal: JOURNAL OF EXPERIMENTAL MEDICINE, 2004, V199, N1 (JAN 5), P35-46
ISSN: 0022-1007 Publication date: 20040105
Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY

10021 USA
Language: English Document Type: ARTICLE
Abstract: Carcinoembryonic antigen-related cell adhesion molecules (CEACAMs) are used by several human pathogens to anchor themselves to or invade host cells. Interestingly, human granulocytes express a specific isoform, CEACAM3, that participates together with CEACAM1 and CEACAM6 in the recognition of CEACAM-binding microorganisms. Here we show that CEACAM3 can direct efficient, opsonin-independent phagocytosis of CEACAM-binding *Neisseria*, *Moraxella*, and *Haemophilus* species. CEACAM3- but not CEACAM6-mediated uptake is blocked by dominant-negative versions of the small GTPase Rac. Moreover, CEACAM3 engagement triggers membrane recruitment and increased GTP loading of Rac that are not observed upon bacterial binding to CEACAM6. Internalization and Rac stimulation are also inhibited by compromising the integrity of an immunoreceptor tyrosine-based activation motif (ITAM)-like sequence

in the cytoplasmic tail of CEACAM3 or by interference with Src family protein tyrosine kinases that phosphorylate CEACAM3. In contrast to interfering with CEACAM6, blockage of CEACAM3-mediated events reduces the ability of primary human granulocytes to internalize and eliminate CEACAM-binding bacteria, indicating an important role of CEACAM3 in the control of human-specific pathogens by the innate immune system.

14/7/34 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

11497457 Genuine Article#: 659XB Number of References: 39
Title: A novel cell-binding mechanism of *Moraxella catarrhalis* ubiquitous

surface protein UspA: specific targeting of the N-domain of carcinoembryonic antigen-related cell adhesion molecules by UspA1
Author(s): Hill DJ; Virji M (REPRINT)
Corporate Source: Univ Bristol,Sch Med Sci, Dept Pathol & Microbiol,Bristol

BS8 1TD/Avon/England/ (REPRINT); Univ Bristol,Sch Med Sci, Dept Pathol

& Microbiol,Bristol BS8 1TD/Avon/England/
Journal: MOLECULAR MICROBIOLOGY, 2003, V48, N1 (APR), P117-129
ISSN: 0950-382X Publication date: 20030400
Publisher: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4 2DG,

OXON, ENGLAND

Language: English Document Type: ARTICLE

Abstract: Carcinoembryonic antigen-related cell adhesion molecules (CEACAMs) are receptors for several *Neisseria* and *Haemophilus* spp. In this investigation, we demonstrate that a major

outer membrane protein of *Moraxella catarrhalis* (Mx) strains, belonging to the ubiquitous surface protein (Usp) family, also interacts with the

receptor. The interaction was demonstrated in Western blot overlay of

SDS-PAGE-separated bacterial proteins using soluble receptor constructs

as well as by co-precipitation experiments. The identity of the bacterial ligand was further ascertained by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS).

It was shown to belong to the UspA1 subfamily. In general, antibodies

raised against synthetic UspA1, but not UspA2, peptides bound to the Mx

ligand. CEACAM1-Fc-binding property could be demonstrated in all

the clinical isolates examined but varied between strains. A single colony derivative of an Mx isolate was also demonstrated to bind to transfected Chinese hamster ovary and some human respiratory epithelial cells in a CEACAM-dependent manner. Thus, we have identified the third respiratory pathogen with the capacity to target the CEACAM family of receptors. The Mx ligand is structurally unrelated to those of Neisseria and Haemophilus.

14/7/35 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

10426845 Genuine Article#: 525LV Number of References: 60
Title: Neisserial binding to CEACAM1 arrests the activation and proliferation of CD4(+) T lymphocytes
Author(s): Boulton IC; Gray-Owen SD (REPRINT)
Corporate Source: Univ Toronto, Dept Med Genet & Microbiol, Med Sci Bldg Rm 4381, 1 Kings Coll Circle/Toronto/ON M5S 1A8/Canada/ (REPRINT); Univ Toronto, Dept Med Genet & Microbiol, Toronto/ON M5S 1A8/Canada/
Journal: NATURE IMMUNOLOGY, 2002, V3, N3 (MAR), P229-236
ISSN: 1529-2908 Publication date: 20020300
Publisher: NATURE AMERICA INC, 345 PARK AVE SOUTH, NEW YORK, NY 10010-1707
USA

Language: English Document Type: ARTICLE

Abstract: Infection with Neisseria gonorrhoeae can trigger an intense inflammatory response, yet there is little specific immune response or development of immune memory. In addition, gonorrhea typically correlates with a transient reduction in T lymphocyte counts in blood, and these populations recover when gonococcal infection is resolved.

Such observations suggest that the gonococci have a suppressive effect on the host immune response. We report here that N. gonorrhoeae Opa proteins were able to bind CEACAM1 expressed by primary CD4(+) T lymphocytes and suppress their activation and proliferation. CEACAM1 bound by gonococcal Opa(52) associated with the tyrosine phosphatases SHP-1 and SHP-2, which implicates the receptor's ITIM (immunoreceptor tyrosine-based inhibitory motif) in this effect.

14/7/36 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

10426840 Genuine Article#: 525LV Number of References: 15
Title: Gonococci cause immunosuppression by engaging a coinhibitory
receptor on T lymphocytes
Author(s): Normark S (REPRINT) ; Albiger B; Jonsson AB
Corporate Source: Karolinska Inst,Ctr Microbiol & Tumor
Biol,Stockholm//Sweden/ (REPRINT); Karolinska Inst,Ctr Microbiol &
Tumor Biol,Stockholm//Sweden/; Swedish Inst Infect Dis
Control,Stockholm//Sweden/
Journal: NATURE IMMUNOLOGY, 2002, V3, N3 (MAR), P210-211
ISSN: 1529-2908 Publication date: 20020300
Publisher: NATURE AMERICA INC, 345 PARK AVE SOUTH, NEW YORK, NY
10010-1707
USA
Language: English Document Type: EDITORIAL MATERIAL
Abstract: Gonococci that bind the coinhibitory receptor CEACAM1
appear to down-regulate the activation and proliferation of
CD4(+) T
cells. Such infection-induced immunosuppression helps explain why
there
is little specific immune response associated with gonococcal
disease.

14/7/37 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

10062255 Genuine Article#: 482PC Number of References: 33
Title: CEACAM is not necessary for Neisseria gonorrhoeae to
adhere to and invade female genital epithelial cells
Author(s): Swanson KV (REPRINT) ; Jarvis GA; Brooks GF; Barham BJ;
Cooper
MD; Griffiss JM
Corporate Source: VA Med Ctr,Ctr Immunochem,San Francisco//CA/94121
(REPRINT); VA Med Ctr,Ctr Immunochem,San Francisco//CA/94121; Univ
Calif San Francisco,Dept Lab Med,San Francisco//CA/94143; So
Illinois
Univ,Dept Med Microbiol & Immunol,Springfield//IL/
Journal: CELLULAR MICROBIOLOGY, 2001, V3, N10 (OCT), P681-691
ISSN: 1462-5814 Publication date: 20011000
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2
ONE,
OXON, ENGLAND
Language: English Document Type: ARTICLE
Abstract: Neisseria gonorrhoeae has a repertoire of up to 11
opacity-associated (Opa) proteins that are adhesins. Most
Opa proteins adhere to CEACAM antigens and when

CEACAM molecules are present on the surface of transfected epithelial cells their binding by Opa is thought to induce invasion of these cells by gonococci. In this study, we investigated whether several malignant epithelial cell lines, normal cervical and fallopian tube epithelial cell cultures, as well as normal tube tissue express several of the CEACAM molecules, and whether gonococci use these molecules for adherence and invasion of these female genital epithelial cells. A primary cervical cell culture and metastatic cervical cell line ME180 both expressed CEACAM as shown by whole cell ELISA and flow cytometry, and increased the surface expression of total CEACAM during incubation with Opa(+) gonococci. Opa(+) gonococci both adhered to and invaded these cells; CEACAM-specific monoclonal antibody (Mab) partially abolished this interaction. Two primary fallopian epithelial tube cell cultures, a primary cervical cell culture and two malignant cell lines, HEC-1-B and HeLa, did not express CEACAM nor was CEACAM mRNA present. No evidence of either intracellular or secreted extracellular CEACAM was found with HEC-1-B and HeLa cells. Opa(+) gonococci both adhered to and invaded CEACAM non-expressing cells; however, Opa(+) gonococcal association with these non-expressing cell lines could not be inhibited with CEACAM-specific Mab. These data show that CEACAM is not always expressed on female genital epithelial cells and is not essential for gonococcal adherence and invasion. However, when CEACAM is expressed, Opa(+) gonococci exploit it for the adherence to and invasion of these cells.

14/7/38 (Item 9 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

09449765 Genuine Article#: 406VU Number of References: 51
Title: The variable P5 proteins of typeable and non-typeable Haemophilus

influenzae target human CEACAM1
Author(s): Hill DJ; Toleman MA; Evans DJ; Villullas S; van Alphen L; Virji

M (REPRINT)
Corporate Source: Univ Bristol,Sch Med Sci, Dept Pathol & Microbiol,Bristol

BS8 1TD/Avon/England/ (REPRINT); Univ Bristol,Sch Med Sci, Dept Pathol
& Microbiol,Bristol BS8 1TD/Avon/England/; Natl Inst Publ Hlth & Environm,RIVM,NL-3720 BA Bilthoven//Netherlands/

Journal: MOLECULAR MICROBIOLOGY, 2001, V39, N4 (FEB), P850-862
ISSN: 0950-382X Publication date: 20010200
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 ONE,

OXON, ENGLAND

Language: English Document Type: ARTICLE

Abstract: *Haemophilus influenzae*, a commensal of the human respiratory mucosa, is an important cause of localized and systemic infections. We

have recently shown that numerous strains of capsulate (typeable) and

acapsulate (non-typeable) *H. influenzae* target the carcinoembryonic

antigen (CEA) family of cell adhesion molecules (CEACAMs).

Moreover, the ligands appeared to be antigenically variable and, when

using viable typeable bacteria, their adhesive functions were inhibited

by the presence of capsule. In this report, we show that the antigenically variable outer membrane protein, P5, expressed by typeable and non-typeable *H. influenzae* targets human CEACAM1.

Variants and mutants lacking the expression of P5 of all strains tested

were unable to target purified soluble receptors. A non-typeable strain

that did not interact with CEACAM1 was made adherent to both the soluble receptors and CEACAM1-transfected Chinese hamster ovary cells by transformation with the P5 gene derived from the adherent typeable strain Rd. However, several *H. influenzae* mutants

lacking P5

expression continued to bind the cell-bound CEACAM1 receptors.

These observations suggest that (i) CEACAM1 alone can support P5 interactions and (ii) some strains contain additional ligands

with the

property to target CEACAM1 but require the receptor in the cellular context. The identification of a common ligand in diverse strains of *H. influenzae* and the presence of multiple ligands for

the

same receptor suggests that targeting of members of the CEACAM family of receptors may be of primary significance in

colonization and

pathogenesis of *H. influenzae* strains.

14/7/39 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

09273455 Genuine Article#: 388GM Number of References: 40
Title: Expression of pathogen-like Opa adhesins in commensal
Neisseria: genetic and functional analysis
Author(s): Toleman M; Aho E; Virji M (REPRINT)

Corporate Source: Univ Bristol,Sch Med Sci, Dept Pathol,Bristol BS8 1TD/Avon/England/ (REPRINT); Univ Bristol,Sch Med Sci, Dept Pathol,Bristol BS8 1TD/Avon/England/; Concordia Coll,Dept Biol,Moorhead//MN/56562

Journal: CELLULAR MICROBIOLOGY, 2001, V3, N1 (JAN), P33-44

ISSN: 1462-5814 Publication date: 20010100

Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 ONE,

OXON, ENGLAND

Language: English Document Type: ARTICLE

Abstract: Several species of commensal *Neisseriae* (Cn) may colonize the human nasopharynx, but little is known about their adhesion mechanisms. We have investigated structural and functional similarities

between adhesins of Cn and of *Neisseria meningitidis* (Nm), also a frequent colonizer of the nasopharynx. In this study, we demonstrate

the expression of Opa-like proteins in nine strains of Cn. Phylogenetic analysis segregated the majority of the Cn Opa in a cluster separated from the pathogenic cluster with a few exceptions.

One Opa, which located within the pathogenic cluster, was strikingly similar (74%) to an Opa of a *Neisseria gonorrhoeae* (Ng) strain and, like Ng, it lacked the extra Y-11 or the

(DKF138)-D-136 triplet insert, which are conserved among many *N. meningitidis* Opa proteins. Most importantly, the majority of the Cn Opa proteins were able to interact with human CEACAM1 (CD66a) molecules, previously identified as receptors for pathogenic

Opa proteins. By the use of CEACAM1 N-domain mutants, we demonstrate that Cn Opa target the same region of the N-domain of the receptor as that used by Nm. Furthermore, Cn strains bound to cell-expressed human CEACAM1. In competition assays, adherent Cn strain C450, exhibiting high affinity for CEACAM1, was not displaced by a Nm isolate and vice versa. But in simultaneous incubation, Nm out-competed the Cn strain. This is the first study to

demonstrate the expression of adhesins in Cn that are structurally and

functionally closely related to pathogenic adhesins. The studies imply

that some Cn have the potential to occupy and thus compete with the

pathogens for receptors on human mucosa, their common and exclusive niche.

08913222 Genuine Article#: 343HC Number of References: 59
Title: Molecular analysis of neisserial Opa protein
interactions with the CEA family of receptors: identification of
determinants contributing to the differential specificities of
binding
Author(s): Popp A; Dehio C; Grunert F; Meyer TF (REPRINT) ; GrayOwen
SD
Corporate Source: MAX PLANCK INST INFEKT BIOL,MOL BIOL ABT,
MONBIJOUSTR
2/D-10117 BERLIN//GERMANY/ (REPRINT); MAX PLANCK INST INFEKT
BIOL,MOL
BIOL ABT/D-10117 BERLIN//GERMANY//; MAX PLANCK INST BIOL,INFEKT
BIOL
ABT/D-72076 TUBINGEN//GERMANY//; UNIV FREIBURG,INST
IMMUNOBIOL/D-79104
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Journal: CELLULAR MICROBIOLOGY, 1999, V1, N2 (SEP), P169-181
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Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2
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Language: English Document Type: ARTICLE

Abstract: The carcinoembryonic antigen (CEA) gene family members,
CEACAM1, CEACAM3, CEACAM5 and CEACAM6, are
bound by the Opa outer membrane proteins of pathogenic
Neisseria spp., whereas CEACAM8 is not. In this study, we
demonstrate that the closely related CEACAM4 and CEACAM7,
which are also members of the CEA family, are not Opa receptors.
We exploited the high conservation between CEACAM6 and
CEACAM8 to generate an extensive set of chimeric receptors in
order to delineate the sequences necessary for Opa binding. Using
a transfection-based infection system, we showed that binding of
Opa(52) involves residues 27-42, which are predicted to form
beta-strand C and short loops adjacent to it, and residues lying
between amino acids 60 and 108 in the amino-terminal domain. The
replacement of residues 27-29 in CEACAM6 with the CEACAM1
or CEACAM5 sequences generated recombinant CEACAM6
receptors that are bound by CEACAM1/CEACAM5-specific
Opa variants. Together, our data demonstrate that Opa
proteins bind to residues exposed on the GFCC' face of the
N-terminal

domain of CEACAM receptors, and identify an amino acid triplet
sequence that is responsible for the differential binding of Opa
proteins to CEACAM1, CEACAM5 and CEACAM6.

14/7/41 (Item 12 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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08746732 Genuine Article#: 324XK Number of References: 43

Title: Carcinoembryonic antigens are targeted by diverse strains of typable

and non-typable Haemophilus influenzae

Author(s): Virji M (REPRINT) ; Evans D; Griffith J; Hill D; Serino L; Hadfield A; Watt SM

Corporate Source: UNIV BRISTOL, DEPT PATHOL & MICROBIOL/BRISTOL BS8 1TD/AVON/ENGLAND/ (REPRINT); UNIV BRISTOL, DEPT BIOCHEM/BRISTOL BS8 1TD/AVON/ENGLAND/; UNIV OXFORD, INST MOL MED, MRC, MOL HAEMATOL UNIT/OXFORD OX3 9DU//ENGLAND/

Journal: MOLECULAR MICROBIOLOGY, 2000, V36, N4 (MAY), P784-795

ISSN: 0950-382X Publication date: 20000500

Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 ONE,

OXON, ENGLAND

Language: English Document Type: ARTICLE

Abstract: Haemophilus influenzae (Hi), a commensal of the human respiratory

mucosa, is an important cause of localized and systemic infections. We

show that distinct strains belonging to typable (THi) and nontypable

(NTHi) H. influenzae target human carcinoembryonic antigens (the membrane associated CEA family of cell adhesion molecules, are now termed CEACAMs). All strains of H. influenzae biogroup aegyptius (Hi-aeg) and more than 70% of THi and NTHi strains tested

specifically

recognize CEACAM1-Fc soluble constructs. Furthermore, transfection of Chinese hamster ovary cells with human CEACAM1 cDNA alone was sufficient for promoting Hi interactions with the transfected cells. The majority of the Hi-aeg strains tested

interacted

with soluble constructs containing only the N-terminal domain. In contrast, several THi and NTHi strains reacted with soluble

constructs

only when additional extracellular A and B domains of the receptor were

present. The use of monoclonal antibodies confirmed that THi and NTHi

strains also interact primarily at the N-domain. We used site-directed

mutants of CEACAM1 that contained substitutions at surface exposed amino acids and a molecular model of the N-domain to

identify

the residues involved in interactions with Hi ligands. The studies show

that a common region exposed at the CFG face of the molecule is targeted by diverse Hi strains. However, mutation at distinct

sites

within this area affected the interactions of distinct strains signifying the potential for tissue tropism via this receptor.

Analyses

of the molecular basis of interaction with human cell lines and

purified CEA show that Hi strains, especially those belonging to Hi-aeg, interact with multiple CEACAMs, Because Neisseria meningitidis (Nm) strains are also known to bind at the CFG face of the receptor, we used Nm and Hi strains in co-infection experiments and demonstrate competition between these mucosal pathogens in colonization of target cells via CEACAMs.

14/7/42 (Item 1 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE
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0004561898 SUPPLIER NUMBER: 2002061933
Neisserial binding to CEACAMI arrests the activation and proliferation of CD4 SUP + T lymphocytes
Boulton I.C.; Gray-Owen S.D.
CORRESP. AUTHOR/AFFIL: Gray-Owen S.D., Dept. of Med. Genetics/Microbiology,
University of Toronto, 1 Kings College Circle, Toronto, Ont. M5S 1A8,
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Journal: Nature Immunology (Nat. Immunol.), v3, n3, (229-236), 2002, United States
PUBLICATION DATE: March 27, 2002 (20020327)
CODEN: NIAMC
ISSN: 1529-2908
DOI: <http://dx.doi.org/10.1038/ni769>
RECORD TYPE: Abstract; New
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 60

Infection with *Neisseria gonorrhoeae* can trigger an intense inflammatory response, yet there is little specific immune response or development of immune memory. In addition, gonorrhea typically correlates with a transient reduction in T lymphocyte counts in blood, and these populations recover when gonococcal infection is resolved. Such observations suggest that the gonococci have a suppressive effect on the host immune response. We report here that *N. gonorrhoeae* Opa proteins were able to bind CEACAMI expressed by primary CD4 SUP + T lymphocytes and suppress their activation and proliferation. CEACAMI bound by gonococcal Opa SUB 52 associated with the tyrosine phosphatases SHP-1 and SHP-2, which implicates the receptor's ITIM (immunoreceptor tyrosine-based inhibitory motif) in this effect.

14/7/43 (Item 1 from file: 98)
DIALOG(R)File 98:General Sci Abs
(c) 2009 The HW Wilson Co. All rts. reserv.

04852211 H.W. WILSON RECORD NUMBER: BGSA02102211
Neisseria gonorrhoeae evades host immunity by switching off T
lymphocytes.
Bradbury, Jane
Lancet (North American edition) (Lancet) v. 359 no9307 (Feb. 23 2002)
p.

681
LANGUAGE: English
COUNTRY OF PUBLICATION: United States

ABSTRACT: In a February 19 online report (Nat. Immunol) Gray-Owen and Boulton described new research on the human pathogen Neisseria gonorrhoeae. The researchers challenged CD4+ lymphocytes with gonococci that did or did not express a CEACAM1 (carcinoembryonic antigen-related cellular adhesion molecule 1)-specific Opa protein. They found that lymphocyte activation and proliferation is switched off when the gonococcal Opa proteins bind to the CEACAM1 receptor on the CD4+ lymphocytes. The results suggest a possible answer to the way that the bacterium may prevent the development of an immunological memory response against itself and shed light on why people with gonorrhea exhibit an increased risk of acquiring other sexually transmitted diseases, including HIV.

14/7/44 (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
(c) format only 2009 Dialog. All rts. reserv.

12638031 PMID: 9426134
Differential Opa specificities for CD66 receptors influence tissue interactions and cellular response to Neisseria gonorrhoeae.
Gray-Owen S D; Lorenzen D R; Haude A; Meyer T F; Dehio C
Max-Planck-Institut für Biologie, Abteilung Infektionsbiologie, Tübingen, Germany.
Molecular microbiology (ENGLAND) Dec 1997, 26 (5) p971-80, ISSN
0950-382X--Print Journal Code: 8712028
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH
Main Citation Owner: NLM

Record type: MEDLINE; Completed

The ability of all 11 variable opacity (Opa) proteins encoded by *Neisseria gonorrhoeae* MS11 to interact directly with the five CD66 antigens was determined. Transfected HeLa cell lines expressing individual

CD66 antigens were infected with recombinant *N. gonorrhoeae* and *Escherichia*

coli strains expressing defined Opas. Based upon the ability of these

bacteria to bind and invade and to isolate specifically CD66 antigens from

detergent-soluble extracts of the corresponding cell lines, distinct

specificity groups of Opa interaction with CD66 were seen. Defining these specificity groups allowed us to assign a specific function for CD66a

in the Opa-mediated interaction of gonococci with two different target cell types, which are both known to co-express multiple CD66

antigens. The competence of individual Opas to interact with CD66a was

strictly correlated with their ability to induce an oxidative response by

polymorphonuclear neutrophils. The same Opa specificity was observed for the level of gonococcal binding to primary endothelial cells after

stimulation with TNF α , which was shown to increase the expression of

CD66a rather than CD66e. As CD66e alone is expressed on other target

tissues of gonococcal pathogenicity, Opa variation probably contributes to the cell tropism displayed by gonococci.

Record Date Created: 19980305

Record Date Completed: 19980305

14/7/95 (Item 2 from file: 154)

DIALOG(R)File 154:MEDLINE(R)

(c) format only 2009 Dialog. All rts. reserv.

12454269 PMID: 9218786 Record Identifier: PMC1169969

CD66 carcinoembryonic antigens mediate interactions between Opa-expressing *Neisseria gonorrhoeae* and human polymorphonuclear phagocytes.

Gray-Owen S D; Dehio C; Haude A; Grunert F; Meyer T F

Max-Planck-Institut für Biologie, Abteilung Infektionsbiologie, Tübingen,

Germany.

EMBO journal (ENGLAND) Jun 16 1997, 16 (12) p3435-45, ISSN

0261-4189--Print Journal Code: 8208664

Publishing Model Print

Document type: Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Other Citation Owner: NLM

Record type: MEDLINE; Completed

Colonization of urogenital tissues by the human pathogen *Neisseria gonorrhoeae* is characteristically associated with purulent exudates of

polymorphonuclear phagocytes (PMNs) containing apparently viable bacteria.

Distinct variant forms of the phase-variable opacity-associated (Opa) outer membrane proteins mediate the non-opsonized binding and

internalization of *N. gonorrhoeae* by human PMNs. Using overlay assays and

an affinity isolation technique, we demonstrate the direct interaction

between Opa52-expressing gonococci and members of the human

carcinoembryonic antigen (CEA) family which express the CD66 epitope.

Gonococci and recombinant *Escherichia coli* strains synthesizing Opa52

showed specific binding and internalization by transfected HeLa cell lines

expressing the CD66 family members BGP (CD66a), NCA (CD66c), CGM1 (CD66d)

and CEA (CD66e), but not that expressing CGM6 (CD66b). Bacterial strains

expressing either no opacity protein or the epithelial cell

invasion-associated Opa50 do not bind these CEA family members.

Consistent

with their different receptor specificities, Opa52-mediated interactions

could be inhibited by polyclonal anti-CEA sera, while Opa50 binding was

instead inhibited by heparin. Using confocal laser scanning microscopy, we

observed a marked recruitment of CD66 antigen by Opa52-expressing gonococci

on both the transfected cell lines and infected PMNs. These data indicate

that members of the CEA family constitute the cellular receptors for the

interaction with, and internalization of, *N. gonorrhoeae*.

Record Date Created: 19970808

Record Date Completed: 19970808

(c) format only 2009 Dialog. All rts. reserv.

12196174 PMID: 8962144 Record Identifier: PMC26225

CGM1a antigen of neutrophils, a receptor of gonococcal opacity proteins.

Chen T; Gotschlich E C
Laboratory of Bacterial Pathogenesis and Immunology,
Rockefeller
University, New York, NY 10021, USA.

Proceedings of the National Academy of Sciences of the United States of

America (UNITED STATES) Dec 10 1996, 93 (25) p14851-6, ISSN 0027-8424

--Print Journal Code: 7505876

Contract/Grant Number: AI 10615; AI; NIAID NIH HHS United States
Publishing Model Print

Document type: Journal Article; Research Support, U.S. Gov't, P.H.S.

Languages: ENGLISH

Main Citation Owner: NLM

Other Citation Owner: NLM

Record type: MEDLINE; Completed

Neisseria gonorrhoeae (GC) or Escherichia coli expressing phase-variable opacity (Opa) protein (Opa+ GC or Opa+ E. coli) adhere to human neutrophils and stimulate phagocytosis, whereas their

counterparts not expressing Opa protein (Opa- GC or Opa- E. coli) do not. Opa + GC or E. coli do not adhere to human lymphocytes and promyelocytic cell lines such as HL-60 cells. The adherence

of Opa + GC to the neutrophils can be enhanced dramatically if the neutrophils are preactivated. These data suggest that the components

binding the Opa+ bacteria might exist in the granules. CGM1a antigen, a transmembrane protein of the carcinoembryonic antigen family, is

exclusively expressed in the granulocytic lineage. The predicted molecular

weight of CGM1a is approximately 30 kDa. We observed specific binding of

OpaI+ E. coli to a 30-kDa band of polymorphonuclear leukocytes lysates. To

prove the hypothesis that the 30-kDa CGM1a antigen from neutrophils was the

receptor of Opa+ bacteria, we showed that a HeLa cell line expressing human CGM1a antigen (HeLa-CGM1a) bound Opa+ E. coli and subsequently engulfed the bacteria. Monoclonal antibodies (COL-1) against CGM1 blocked

the interaction between Opa+ E. coli and HeLa-CGM1a. These results demonstrate that HeLa cells when expressing the CGM1a antigens bind and

internalize OpaI+ bacteria.

Record Date Created: 19970115

Record Date Completed: 19970115
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Set	Items	Description
S1	369	AU=GORRINGE, ?
S2	189	AU= REDDIN, ?
S3	114	AU=GRAY-OWEN, ?
S4	3106	AU=BOULTON, ?
S5	3702	S1 OR S2 OR S3 OR S4
S6	196	S5 AND NEISSERIA
S7	198	S5 AND NEISSERIA?
S8	97	RD S7 (unique items)
S9	24	S8 AND (OPA OR CEACAM OR BLEB OR VESSICLE)
S10	0	CEADAM AND OPA AND NEISSERIA?
S11	368	CEACAM? AND OPA AND NEISSERIA?
S12	74	RD S11 (unique items)
S13	68	S12 NOT S9
S14	46	S13 NOT PY>2005

? s (opa (5n) deficient) or (opa (5n) deletion) or (opa (5n) mutant)

12195	OPA
1127740	DEFICIENT
7	OPA(5N)DEFICIENT
12195	OPA
929615	DELETION
23	OPA(5N)DELETION
12195	OPA
1783063	MUTANT
44	OPA(5N)MUTANT
S15	70 (OPA (5N) DEFICIENT) OR (OPA (5N) DELETION) OR (OPA (5N) MUTANT)

? rd s15

>>>Duplicate detection is not supported for File 393.

>>>Records from unsupported files will be retained in the RD set.

S16 13 RD S15 (unique items)

? t s16/7/all

>>>Format 7 is not valid in file 143

16/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0019587579 BIOSIS NO.: 200700247320

The Zic family member, odd-paired, regulates the Drosophila BMP, decapentaplegic, during adult head development

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JOURNAL: Development (Cambridge) 134 (7): p1301-1310 APR 1 2007 2007
ISSN: 0950-1991
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The eye/antennal discs of *Drosophila* form most of the adult head

capsule. We are analyzing the role of the BMP family member decapentaplegic (*dpp*) in the process of head formation, as we have identified a class of cis-regulatory *dpp* mutations (*dpp(s-hc)*) that specifically disrupts expression in the lateral peripodial epithelium of

eye/antennal discs and is required for ventral head formation. Here we

describe the recovery of mutations in odd-paired (*opa*), a zinc finger

transcription factor related to the vertebrate *Zic* family, as dominant

enhancers of this *dpp* head mutation. A single loss-of-function *opa* allele

in combination with a single copy of a *dpp(s-hc)* produces defects in the

ventral adult head. Furthermore, postembryonic loss of *opa* expression

alone causes head defects identical to loss of *dpp(s-hc)/dpp(s-hc)*, and

dpp(hc)/+;opa/+ mutant combinations. *opa* is required

for *dpp* expression in the lateral peripodial epithelium, but not other

areas of the eye/antennal disc. Thus a pathway that includes *opa* and *dpp*

expression in the peripodial epithelium is crucial to the formation of

the ventral adult head. *Zic* proteins and members of the BMP pathway are

crucial for vertebrate head development, as mutations in them are associated with midline defects of the head. The interaction of these

genes in the morphogenesis of the fruitfly head suggests that the regulation of head formation may be conserved across metazoans.

16/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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16656955 BIOSIS NO.: 200200250466
Recombinational error and deletion formation in *Neisseria gonorrhoeae*: A

role for RecJ in the production of pilel deletions
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University, DeKalb, IL, 60115, USA**USA
JOURNAL: MGG Molecular Genetics and Genomics 266 (6): p962-972
February,
2002 2002
MEDIUM: print
ISSN: 1617-4615
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Genetic linkage within *Neisseria gonorrhoeae* populations is in equilibrium, yet the physical linkage map indicates a relatively stable chromosome structure, despite an apparently vast potential for mispairing between repeated sequences (e.g. between the multiple pil or opa alleles, or through mispairing of any of the numerous small repeated sequences that are liberally scattered throughout the chromosome). Therefore, the stability of the physical linkage map suggests that aberrant recombination between repeated sequences is a rare event. This study was undertaken to explore some of the parameters that may govern deletion events between short direct oligonucleotide repeats, using a chromosomal locus that appears to be especially prone to deletions (the pilin expression locus; pilE). In this report, we demonstrate that deletion formation at pilE occurs primarily through recombinational error following a pilE/pilS interaction; illegitimate (i.e. RecA-independent) events can occur, but they are infrequent. In contrast, when genetically engineered opa deletion substrates were constructed and placed in the chromosome, deletions at the opa loci were infrequent even under rec+ conditions. A model is presented in which the gonococcal RecA and RecJ proteins promote pilE deletions through a recombination event that is templated or stabilised by a pilE/pilS interaction.

16655836 BIOSIS NO.: 200200249347

Carcinoembryonic antigen family receptor recognition by gonococcal Opa proteins requires distinct combinations of hypervariable Opa protein domains

AUTHOR: Bos Martine P (Reprint); Kao David; Hogan Daniel M; Grant Christopher C R; Belland Robert J

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Padualaan 8, 3584 CH, Utrecht, Netherlands**Netherlands

JOURNAL: Infection and Immunity 70 (4): p1715-1723 April, 2002 2002

MEDIUM: print

ISSN: 0019-9567

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Neisserial Opa proteins function as a family of adhesins that

bind heparan sulfate proteoglycan (HSPG) or carcinoembryonic antigen family (CEACAM) receptors on human host cells. In order to define the

CEACAM binding domain on Opa proteins, we tested the binding properties

of a series of gonococcal (strain MS11) recombinants producing mutant and chimeric Opa proteins with alterations in one or more of the four surface-exposed loops. Mutagenesis demonstrated that the

semivariable domain, present in the first loop, was completely dispensable for CEACAM binding. In contrast, the two hypervariable (HV)

regions present in the second and third loops were essential for binding;

deletion of either domain resulted in loss of receptor recognition. Deletion of the fourth loop resulted in a severe decrease in Opa expression at the cell surface and could therefore not be tested for CEACAM binding. Chimeric Opa variants, containing combinations of HV regions derived from different CEACAM binding Opa proteins, lost most of

their receptor binding activity. Some chimeric variants gained HSPG binding activity. Together, our results indicate that full recognition of

CEACAM receptors by Opa proteins requires a highly coordinate interplay

between both HV regions. Furthermore, shuffling of HV regions may result

in novel HSPG receptor binding activity.

16/7/4 (Item 4 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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16526565 BIOSIS NO.: 200200120076

Association studies of the HOPA dodecamer duplication variant in different

subtypes of autism

AUTHOR: Beyer Kim S; Klauck Sabine M; Benner Axel; Poustka Fritz; Poustka

Annemarie (Reprint)

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JOURNAL: American Journal of Medical Genetics 114 (1): p110-115

January 8,

2002 2002

MEDIUM: print

ISSN: 0148-7299

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The HOPA gene in Xq13 is coding for a protein involved in a nuclear thyroid receptor complex. Previous studies suggested association

of the dodecamer duplication in the OPA-repeat region in exon 43 (according to the genomic database sequence) with autism, mental retardation, and schizophrenia/hypothyroidism. We determined the frequency of this 12 bp duplication variant in a sample of 155 patients

divided in different subtypes of autism, 278 parents of those patients,

and 157 control individuals. The allele frequency of the duplication variant was not significantly different between autistic patients, their

parents, and the control group. Therefore, it is unlikely that this 12 bp

duplication variant of the HOPA gene has major relevance to the susceptibility to different subtypes of autism at least in this German

patient sample. In addition, we identified a third variant with a 15 bp

deletion in the OPA-repeat region, recently described by another group, in one autistic patient. This third allele was also present in the patient's nonautistic mother and sister, who are heterozygous for this variant, but could not be detected in any other

individual genotyped in this study. Expression analysis revealed transcription of all three allelic variants in lymphoblastoid cell lines.

Furthermore, we identified a new splice variant that utilizes an additional 9 bp of the 3' intron subsequent to exon 39. Both alternative

transcripts are coexpressed in all fetal and adult tissues examined.

16/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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15068380 BIOSIS NO.: 199900328040

A *Neisseria gonorrhoeae* immunoglobulin A1 protease mutant is infectious in

the human challenge model of urethral infection

AUTHOR: Johannsen Diana B; Johnston David M; Koymen Hakan O; Cohen Myron S;

Cannon Janne G (Reprint)

AUTHOR ADDRESS: Department of Microbiology and Immunology, University of

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USA**USA

JOURNAL: Infection and Immunity 67 (6): p3009-3013 June, 1999 1999

MEDIUM: print

ISSN: 0019-9567

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Many mucosal pathogens, including *Neisseria gonorrhoeae*, produce

proteases that cleave immunoglobulin A (IgA), the predominant immunoglobulin class produced at mucosal surfaces. While

considerable

circumstantial evidence suggests that IgA1 protease contributes to gonococcal virulence, there is no direct evidence that *N.*

gonorrhoeae

requires IgA1 protease activity to infect a human host. We

constructed a

N. gonorrhoeae iga mutant without introducing new antibiotic resistance

markers into the final mutant strain and used human experimental infection to test the ability of the mutant to colonize the male

urethra

and to cause gonococcal urethritis. Four of the five male volunteers inoculated with the Iga- mutant became infected. In every

respect-clinical signs and symptoms, incubation period between inoculation and infection, and the proportion of volunteers

infected-the

outcome of human experimental infection with FA1090iga was indistinguishable from that previously reported for a variant of

parent

strain FA1090 matching the mutant in expression of Opa proteins, lipooligosaccharide, and pilin. These results indicate that *N.*

gonorrhoeae does not require IgA1 protease production to cause

experimental urethritis in males.

16/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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14300690 BIOSIS NO.: 199800094937

Using the yeast two-hybrid system to identify human epithelial cell proteins that bind gonococcal Opa proteins: Intracellular gonococci bind

pyruvate kinase via their Opa proteins and require host pyruvate for growth

AUTHOR: Williams John M; Chen Gi-Chung; Zhu Li; Rest Richard F
(Reprint)

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JOURNAL: Molecular Microbiology 27 (1): p171-186 Jan., 1998 1998

MEDIUM: print

ISSN: 0950-382X

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Neisseria gonorrhoeae opacity-associated (Opa) proteins are
a

family of outer membrane proteins involved in gonococcal adherence
to and

invasion of human cells. We wanted to identify additional roles for
Opa

in the infectious process and used the yeast two-hybrid system to
identify human epithelial cell proteins that interact with Opa
proteins.

Although this system has been used successfully to identify many
types of

interacting proteins, it has not been used to screen a human cell
cDNA

library for binding partners of a prokaryotic outer membrane
protein.

Therefore, we were also interested in exploring the versatility of
the

yeast two-hybrid system in identifying bacteria-host interactions.
Using

OpaP from strain F62SF as bait, we screened a HeLa cell cDNA
library for

Opa-interacting proteins (OIPs). We identified five different OIPs,
designated OIP1-OIP5, two of which are homologous to human proteins

-
thyroid hormone receptor interacting protein (TRIP6) and pyruvate
kinase

isoenzyme M2 (PK). In the studies presented here, we investigated the interaction between Opa proteins and PK in more depth. Opa-PK interactions were confirmed by in vitro and in vivo assays independent of the yeast two-hybrid system. Escherichia coli expressing six different Opa proteins from gonococcal strain FA1090 all bound more PK than Opa-negative E. coli in in vitro binding assays. Using anti-PK antibody and fluorescence microscopy, we showed that human epithelial cell PK co-localizes with intracellular Opa+ gonococci and E. coli expressing Opa proteins. Using a mutant of N. gonorrhoeae unable to grow on pyruvate or lactate, it appears that intracellular pyruvate is essential for gonococcal growth and survival. These results suggest a novel mechanism in bacterial pathogenesis, i.e. the requirement for direct molecular interaction with a host metabolic enzyme (PK) for the acquisition of an essential intracellular carbon source and growth substrate (pyruvate). These results demonstrate that the yeast two-hybrid system is a valuable tool for identifying biologically relevant interactions between bacteria and host proteins, providing valuable leads for further investigations into novel mechanisms of bacterial pathogenesis.

16/7/7 (Item 1 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0002333573 IP ACCESSION NO: 5390328
Recombinational error and deletion formation in Neisseria gonorrhoeae: a role for RecJ in the production of pilE sub(L) deletions

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DeKalb, IL
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Molecular Genetics and Genomics, v 266, n 6, p 962-972, February 2002
PUBLICATION DATE: 2002

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DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 1617-4615
DOI: 10.1007/s00438-001-0618-5
FILE SEGMENT: Genetics Abstracts; Bacteriology Abstracts
(Microbiology B)

ABSTRACT:

Genetic linkage within *Neisseria gonorrhoeae* populations is in equilibrium, yet the physical linkage map indicates a relatively stable chromosome structure, despite an apparently vast potential for mispairing between repeated sequences (e.g. between the multiple pil or opa alleles, or through mispairing of any of the numerous small repeated sequences that are liberally scattered throughout the chromosome). Therefore, the stability of the physical linkage map suggests that aberrant recombination between repeated sequences is a rare event. This study was undertaken to explore some of the parameters that may govern deletion events between short direct oligonucleotide repeats, using a chromosomal locus that appears to be especially prone to deletions (the pilin expression locus; pilE). In this report, we demonstrate that deletion formation at pilE occurs primarily through recombinational error following a pilE/pilS interaction; illegitimate (i.e. RecA-independent) events can occur, but they are infrequent. In contrast, when genetically engineered opa deletion substrates were constructed and placed in the chromosome, deletions at the opa loci were infrequent even under rec super(+) conditions. A model is presented in which the gonococcal RecA and RecJ proteins promote pilE deletions through a recombination event that is templated or stabilised by a pilE/pilS interaction.

16/7/8 (Item 2 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0001960181 IP ACCESSION NO: 4491331
Mutagenesis of the *Neisseria gonorrhoeae* porin reduces invasion in epithelial cells and enhances phagocyte responsiveness

Bauer, FJ; Rudel, T; Stein, M; Meyer, TF*
Max-Planck-Institut fuer Biologie, Abt Infektionsbiologie,
Spemannstrasse
34, 72076 Tuebingen, Germany, [mailto:meyer@mpiib-berlin.mpg.de]

Molecular Microbiology, v 31, n 3, p 903-913, February 1999
PUBLICATION DATE: 1999

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0950-382X
FILE SEGMENT: Nucleic Acids Abstracts; Bacteriology Abstracts
(Microbiology
B)

ABSTRACT:

Porin (PorB), the major outer membrane protein of *Neisseria gonorrhoeae*, has been implicated in pathogenesis previously. However, the fact that porin deletion mutants are not viable has complicated investigations. Here, we describe a method of manipulating the porin gene site-specifically. *N. gonorrhoeae* MS11, which harbours the porB sub(1B) (P.1B) porin allele, was used to generate mutants carrying deletions in the surface loops 1 and 5. An 11-amino-acid deletion in loop 1 impaired Opa sub(50)-dependent invasion into human Chang epithelial cells, whereas loop 5 deletion exhibited no apparent phenotype. In a second approach, the complete gonococcal porB sub(1B) was replaced by the porB sub(N1a) gene of *Neisseria lactamica*. Such mutants were unable to induce efficient uptake by epithelial cells but induced an enhanced respiratory response in HL60 phagocytic cells. The increased respiratory burst was accompanied by an enhanced phagocytic uptake of the mutant compared with the wild-type strain. Our data extend previous evidence for multiple central functions of PorB in the infection process.

16/7/9 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

15294924 Genuine Article#: 057JJ Number of References: 61
Title: alpha-2,3-sialyltransferase enhances *Neisseria gonorrhoeae* survival

during experimental murine genital tract infection
Author(s): Wu H; Jerse AE (REPRINT)
Corporate Source: Uniformed Serv Univ Hlth Sci, Dept Microbiol & Immunol, 4301 Jones Bridge Rd/Bethesda//MD/20814 (REPRINT);
Uniformed

Serv Univ Hlth Sci, Dept Microbiol & Immunol, Bethesda//MD/20814 (ajerse@usuhs.mil)

Journal: INFECTION AND IMMUNITY, 2006, V74, N7 (JUL), P4094-4103

ISSN: 0019-9567 Publication date: 20060700

Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904

USA

Language: English Document Type: ARTICLE

Abstract: The addition of host-derived sialic acid to *Neisseria gonorrhoeae*

lipooligosaccharide is hypothesized to be an important mechanism by

which gonococci evade host innate defenses. This hypothesis is based

primarily on in vitro assays of complement-mediated and phagocytic killing. Here we report that a nonpolar alpha-2,3-sialyltransferase

(*lst*) mutant of *N. gonorrhoeae* was significantly attenuated in its capacity to colonize the lower genital tract of 17-beta estradiol-treated female BALB/c mice during competitive infection

with the wild-type strain. Genetic complementation of the *lst* mutation restored recovery of the mutant to wild-type levels. Studies with B10.D2-HC(o)H2(d)H(2)-T18c/OSN (C5-deficient) mice showed that attenuation of the *lst* mutant was not due to increased

sensitivity to complement-mediated bacteriolysis, a result that is consistent with

recently reported host restrictions in the complement cascade. However,

lst-deficient gonococci were killed more rapidly than sialylated wild-type gonococci following intraperitoneal injection into normal

mice, which is consistent with sialylation conferring protection against killing by polymorphonuclear leukocytes (PMNs). As reported for

human PMNs, sialylated gonococci were more resistant to killing by murine PMNs, and sialylation led to reduced association with and induction of a weaker respiratory burst in PMNs from

estradiol-treated mice. In summary, these studies suggest sialylation confers a survival

advantage to *N. gonorrhoeae* in mice by increasing resistance to PMN

killing. This report is the first direct demonstration that alpha-2,3-sialyltransferase contributes to *N. gonorrhoeae* pathogenesis in

an in vivo model. This study also validates the use of experimental

murine infection to study certain aspects of gonococcal pathogenesis.

16/7/10 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

15002012 Genuine Article#: 0280Y Number of References: 20
Title: Using orthogonal projection approach (OPA) for rank-deficient reaction processes
Author(s): Xu CJ; Gourvenec S; Liang YZ; Massart DL (REPRINT)
Corporate Source: Vrije Univ Brussels, Inst Pharmaceut, ChemoAC, Laarbeeklaan 103/B-1090 Brussels//Belgium/ (REPRINT); Vrije Univ Brussels, Inst Pharmaceut, ChemoAC, B-1090 Brussels//Belgium/; Cent S Univ Technol, Coll Chem & Chem Engrg, Changsha 410083//Peoples R China/(fabi@vub.ac.be)
Journal: CHEMOMETRICS AND INTELLIGENT LABORATORY SYSTEMS, 2006, V81, N1 (MAR 15), P3-12
ISSN: 0169-7439 Publication date: 20060315
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
Language: English Document Type: ARTICLE
Abstract: Orthogonal projection approach (OPA) has been used for monitoring batch processes. However, because of the mass balance constraints between the reactants and products in a chemical reaction, standard OPA will fail if rank-deficiency occurs. The effect of the rank-deficiency on using OPA for process reaction data sets is discussed, and a new automatic approach for resolution of rank-deficiency data sets by OPA is proposed for batch control. The method is demonstrated for an industrial batch data set. (c) 2005 Elsevier B.V. All rights reserved.

16/7/11 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

10519137 Genuine Article#: 535AJ Number of References: 55
Title: Recombinational error and deletion formation in *Neisseria gonorrhoeae*: a role for RecJ in the production of pilE(L) deletions
Author(s): Hill SA (REPRINT) ; Grant CCR
Corporate Source: No Illinois Univ, Dept Biol Sci, De Kalb//IL/60115 (REPRINT); No Illinois Univ, Dept Biol Sci, De Kalb//IL/60115; NIAID, Rocky Mt Labs, Microbial Struct & Funct Lab, NIH, Hamilton//MT/59840
Journal: MOLECULAR GENETICS AND GENOMICS, 2002, V266, N6 (FEB), P962-972

ISSN: 1617-4615 Publication date: 20020200
Publisher: SPRINGER-VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010 USA
Language: English Document Type: ARTICLE
Abstract: Genetic linkage within *Neisseria gonorrhoeae* populations is in

equilibrium., yet the physical linkage map indicates a relatively stable chromosome structure, despite an apparently vast potential for mispairing between repeated sequences (e.g. between the multiple pil or opa alleles, or through mispairing of any of the numerous small repeated sequences that are liberally scattered throughout the chromosome). Therefore, the stability of the physical linkage map suggests that aberrant recombination between repeated sequences is a rare event. This study was undertaken to explore some of the parameters that may govern deletion events between short direct oligonucleotide repeats. using a chromosomal locus that appears to be especially prone to deletions (the pilin expression locus. pilE). In this report., we demonstrate that deletion formation at pilE occurs primarily through recombinational error following a pilE/pilS interaction, illegitimate (i.e. RecA-independent) events can occur, but they are infrequent. In contrast, when genetically engineered opa deletion substrates were constructed and placed in the chromosome, deletions at the opa loci were infrequent even under rec(+) conditions. A model is presented in which the gonococcal RecA and RecJ proteins promote pilE deletions through a recombination event that is templated or stabilised by a pilE/pilS interaction.

16/7/12 (Item 1 from file: 65)
DIALOG(R)File 65:Inside Conferences
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02092122 INSIDE CONFERENCE ITEM ID: CN021920088
Construction, characterization, and analysis of chimeric and deletion mutant Opa proteins in *N. gonorrhoeae*
Grant, C. C. R.; Bos, M. P.; Swanson, J.; Belland, R. J.
CONFERENCE: Microbial pathogenesis and host response-Meeting
ABSTRACTS OF PAPERS PRESENTED AT THE COLD SPRING HARBOR MEETING ON
MICROBIAL PATHOGENESIS AND HOST RESPONSE, 1997 P: 43

Cold Spring Harbor Laboratory, 1997

LANGUAGE: English DOCUMENT TYPE: Conference Abstracts

CONFERENCE LOCATION: Cold Spring Harbor, NY

CONFERENCE DATE: Sep 1997 (199709)

16/7/13 (Item 1 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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137274084 CA: 137(19)274084m PATENT

Non-virulent recombinant type III Yersinia strains with multiple mutation

in effector and invasin genes for heterologous therapeutic protein delivery

INVENTOR(AUTHOR): Cornelis, Guy

LOCATION: Belg.

ASSIGNEE: Universite Catholique De Louvain

PATENT: PCT International ; WO 200277249 A2 DATE: 20021003

APPLICATION: WO 2002EP3372 (20020326) *EP 2001870064 (20010326)

PAGES: 49 pp. CODEN: PIXXD2 LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: C12N-136/A

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW ; MZ; SD; SL; SZ; TZ; UG; ZM; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG

SECTION:

CA203002 Biochemical Genetics

CA201XXX Pharmacology

CA210XXX MICROBIAL, ALGAL, AND FUNGAL BIOCHEMISTRY

CA215XXX Immunochemistry

CA263XXX Pharmaceuticals

IDENTIFIERS: eukaryote protein delivery nonvirulent recombinant Yersinia

effector invasin mutation, vaccine delivery gene targeting nonvirulent

type III Yersinia

DESCRIPTORS:

Vaccines...
adjuvant, Yersinia mutant delivered; non-virulent recombinant type III
Yersinia strains with multiple mutation in effector and invasin genes
for heterologous therapeutic protein delivery

Proteins...
AFA, for Yersinia mutant surface targeting; non-virulent recombinant
type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Toxins...
anthrax, EF; non-virulent recombinant type III Yersinia strains with
multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Toxins...
anthrax, LF; non-virulent recombinant type III Yersinia strains with
multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Drug delivery systems...
carriers, for Yersinia mutant related drugs; non-virulent recombinant
type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Human... Neoplasm...
cell of, Yersinia mutant for protein delivery to; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Antigens...
cell specific, recognized by antibody expressed from recombinant Yersinia; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Toxins...
cholera, A1; non-virulent recombinant type III Yersinia strains with
multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Intestine...
colon, disease, treatment using Yersinia mutant delivered drugs; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Transcription factors...
CREB (cAMP-responsive element-binding), inhibiting inflammation mediated by; non-virulent recombinant type III Yersinia strains with
multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Intestine,disease...

- Crohn's, treatment using Yersinia mutant delivered drugs;
- non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein d

Medicine...

- delivery; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

T cell(lymphocyte)...

- detection of the response to Yersinia mutant delivered drugs;
- non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous

therapeutic

- prote

Drug delivery systems...

- diluent, for Yersinia mutant related drugs; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Toxins...

- diphtheria, dtxA; non-virulent recombinant type III Yersinia strains

- with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Infection...

- epitope related to; non-virulent recombinant type III Yersinia strains

- with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Proteins...

- ERK, inhibiting inflammation mediated by; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Drug delivery systems...

- excipient, for Yersinia mutant related drugs; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Plasmid vectors...

- expressing heterologous protein expression; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Ovary...

- follicle cell, Yersinia mutant for protein delivery to;
- non-virulent recombinant type III Yersinia strains with multiple mutation in

effector and invasin genes for heterologous therapeutic protein
del
Lipopolysaccharides...
for T cell detection of the response to Yersinia mutant delivered
drugs; non-virulent recombinant type III Yersinia strains with
multiple
mutation in effector and invasin genes for heterologous therap
Test kits...
for the detection of the immune response to Yersinia mutant
delivered
drugs; non-virulent recombinant type III Yersinia strains with
multiple
mutation in effector and invasin genes for heterologous th
Signal peptides... Adhesins...
for Yersinia mutant surface targeting; non-virulent recombinant
type
III Yersinia strains with multiple mutation in effector and
invasin
genes for heterologous therapeutic protein delivery
Proteins...
IkB, inhibiting inflammation mediated by; non-virulent
recombinant type III Yersinia strains with multiple mutation in
effector and invasin genes for heterologous therapeutic protein
delivery
Mutation...
in Yersinia effector or invasin gene; non-virulent recombinant
type III
Yersinia strains with multiple mutation in effector and invasin
genes
for heterologous therapeutic protein delivery
Immunity...
induction to Yersinia mutant delivered drugs; non-virulent
recombinant
type III Yersinia strains with multiple mutation in effector and
invasin genes for heterologous therapeutic protein delivery
Eukaryota...
infected or inflamed, Yersinia mutant for protein delivery to;
non-virulent recombinant type III Yersinia strains with multiple
mutation in effector and invasin genes for heterologous
therapeutic
prot
Drug delivery systems...
injections, i.m., for Yersinia mutant related drugs; non-virulent
recombinant type III Yersinia strains with multiple mutation in
effector and invasin genes for heterologous therapeutic protein
delive
Drug delivery systems...
injections, i.p., for Yersinia mutant related drugs; non-virulent
recombinant type III Yersinia strains with multiple mutation in
effector and invasin genes for heterologous therapeutic protein
delive
Drug delivery systems...

injections, s.c., for Yersinia mutant related drugs; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein deliver

Drug delivery systems...
intradermal, for Yersinia mutant related drugs; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Drug delivery systems...
intralymphoidal, for Yersinia mutant related drugs; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein deliver

Drug delivery systems...
intraepiurial, for Yersinia mutant related drugs; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Drug delivery systems...
intrathecal, for Yersinia mutant related drugs; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Drug delivery systems...
intratumoral, for Yersinia mutant related drugs; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Gene,microbial...
inv, mutation of; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Proteins...
invasins, gene inv or yadA, mutation of; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Proteins...
JNK, inhibiting inflammation mediated by; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Gene,microbial...
linked to the iron acquisition system, mutation of; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein deliver

Proteins...

- MAPK, inhibiting inflammation mediated by; non-virulent recombinant type III *Yersinia* strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Proteins...

- MAPKK, inhibiting inflammation mediated by; non-virulent recombinant type III *Yersinia* strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Histocompatibility antigens...

- MHC (major histocompatibility complex), antigens coupled to *Yersinia* mutant delivered; non-virulent recombinant type III *Yersinia* strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Pseudomonas aeruginosa... *Burkholderia cepacia*... *Chlamydia*...

- mutant strain for drug delivery; non-virulent recombinant type III *Yersinia* strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Transcription factors...

- NF- κ B (nuclear factor κ B), inhibiting inflammation mediated by; non-virulent recombinant type III *Yersinia* strains with multiple mutation in effector and invasin genes for heterologous the *Yersinia enterocolitica*... Promoter(genetic element)... Toxins...

Epitopes

- ... Antigens... *Yersinia pseudotuberculosis*... *Yersinia*...

Anti-inflammatory agents... Inflammation...

- non-virulent recombinant type III *Yersinia* strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Proteins...

- OPA, for *Yersinia* mutant surface targeting; non-virulent recombinant type III *Yersinia* strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Drug delivery systems...

- ophthalmic, for *Yersinia* mutant related drugs; non-virulent recombinant type III *Yersinia* strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Lymphocyte...

- peripheral blood, for the immune response detection; non-virulent recombinant type III *Yersinia* strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

delive

Plasmid vectors...

- pIML421, for multiple-mutant *Yersinia* strain preparation; non-virulent

recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Proteins...

- p38, inhibiting inflammation mediated by; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Antibodies...

- recognizing cell marker, for Yersinia mutant surface targeting; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Plasmid vectors...

- suicide, for multiple-mutant Yersinia strain preparation; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Autoimmune disease... Digestive tract...

- treatment using Yersinia mutant delivered drugs; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Antigens...

- tumor-associated; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Gene, microbial...

- yadA, mutation of; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Eukaryota... Plant cell... Antigen-presenting cell... B cell (lymphocyte)...

Dendritic cell... Macrophage... Monocyte... Fibroblast...

- Yersinia mutant for protein delivery to; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Proteins... Peptides, biological studies... Lipids, biological studies...

- Yersinia mutant targeted to; non-virulent recombinant type III Yersinia strains with multiple mutation in effector and invasin genes for heterologous therapeutic protein delivery

Gene, microbial...

- YIPa, mutation of; non-virulent recombinant type III Yersinia strains

with multiple mutation in effector and invasin genes for
 heterologous
 therapeutic protein delivery
 Gene,microbial...
 YomA, mutation of; non-virulent recombinant type III Yersinia
 strains
 with multiple mutation in effector and invasin genes for
 heterologous
 therapeutic protein delivery
 Gene,microbial...
 yopA, mutation of; non-virulent recombinant type III Yersinia
 strains
 with multiple mutation in effector and invasin genes for
 heterologous
 therapeutic protein delivery
 Gene,microbial...
 yopE, mutation of; non-virulent recombinant type III Yersinia
 strains
 with multiple mutation in effector and invasin genes for
 heterologous
 therapeutic protein delivery
 Gene,microbial...
 yopH, mutation of; non-virulent recombinant type III Yersinia
 strains
 with multiple mutation in effector and invasin genes for
 heterologous
 therapeutic protein delivery
 Gene,microbial...
 yopJ, mutation of; non-virulent recombinant type III Yersinia
 strains
 with multiple mutation in effector and invasin genes for
 heterologous
 therapeutic protein delivery
 Gene,microbial...
 yopM, mutation of; non-virulent recombinant type III Yersinia
 strains
 with multiple mutation in effector and invasin genes for
 heterologous
 therapeutic protein delivery
 ? ds

Set	Items	Description
S1	369	AU=GORRINGE, ?
S2	189	AU= REDDIN, ?
S3	114	AU=GRAY-OWEN, ?
S4	3106	AU=BOULTON, ?
S5	3702	S1 OR S2 OR S3 OR S4
S6	196	S5 AND NEISSERIA
S7	198	S5 AND NEISSERIA?
S8	97	RD S7 (unique items)
S9	24	S8 AND (OPA OR CEACAM OR BLEB OR VESSICLE)
S10	0	CEADAM AND OPA AND NEISSERIA?

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S11      368    CEACAM? AND OPA AND NEISSERIA?
S12      74     RD S11  (unique items)
S13      68     S12 NOT S9
S14      46     S13 NOT PY>2005
S15      70     (OPA (5N) DEFICIENT) OR (OPA (5N) DELETION) OR (OPA
(5N) M-

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UTANT)

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S16      13     RD S15  (unique items)
? ds

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Set      Items  Description
S1       369    AU=GORRINGE, ?
S2       189    AU= REDDIN, ?
S3       114    AU=GRAY-OWEN, ?
S4       3106   AU=BOULTON, ?
S5       3702   S1 OR S2 OR S3 OR S4
S6       196    S5 AND NEISSERIA
S7       198    S5 AND NEISSERIA?
S8       97     RD S7  (unique items)
S9       24     S8 AND (OPA OR CEACAM OR BLEB OR VESSICLE)
S10      0      CEADAM AND OPA AND NEISSERIA?
S11      368    CEACAM? AND OPA AND NEISSERIA?
S12      74     RD S11  (unique items)
S13      68     S12 NOT S9
S14      46     S13 NOT PY>2005
S15      70     (OPA (5N) DEFICIENT) OR (OPA (5N) DELETION) OR (OPA
(5N) M-

```

UTANT)

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S16      13     RD S15  (unique items)
? s opacity and protein and (deficient or deletion or mutant) and
Neisseria

```

```

          72020  OPACITY
15947008  PROTEIN
1127740   DEFICIENT
929615    DELETION
1783063   MUTANT
143415    NEISSERIA

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S17      99     OPACITY AND PROTEIN AND (DEFICIENT OR DELETION OR
MUTANT)
          AND NEISSERIA
? rd s17

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>>>Duplicate detection is not supported for File 393.

>>>Records from unsupported files will be retained in the RD set.

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S18      30     RD S17  (unique items)
? t s18/7/all

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>>>Format 7 is not valid in file 143

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18/7/1    (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0019507264 BIOSIS NO.: 200700167005

DC-SIGN (CD209) recognition of *Neisseria gonorrhoeae* is circumvented by lipooligosaccharide variation

AUTHOR: Zhang Pei; Schwartz Olivier; Pantelic Milica; Li Geling; Knazze

Quita; Nobile Cinzia; Radovich Milan; He Johnny; Hong Soon-Cheol; Klena

John (Reprint); Chen Tie

AUTHOR ADDRESS: US Naval Med Res Unit 3, Enter Dis Res Program, PSC452, Box

154, FPO AE 09835, Cairo, Egypt**Egypt

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JOURNAL: Journal of Leukocyte Biology 79 (4): p731-738 APR 2006 2006

ISSN: 0741-5400

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: *Neisseria gonorrhoeae* (GC) or *Escherichia coli* HB101 (hereafter referred to as *E. coli*) expressing opacity (Opa) proteins adhere to human host cells and stimulate phagocytosis as a result of the interaction of certain Opa proteins to carcinoembryonic antigen-related cellular adhesion molecule 1 (CEACAM1; CD66a) receptors.

Our experiments show that the Opa-CEACAM1 interaction does not play a

significant role in adherence between these bacteria and dendritic cells

(DCs). Instead, phagocytosis of GC and *E. coli* by DCs is mediated by the

DC-specific intercellular adhesion molecule-grabbing nonintegrin, (SIGN;

CD209) receptor. DC-SIGN recognition and subsequent phagocytosis of GC

are limited, however, to a lipooligosaccharide (LOS) mutant (lgtB) of GC. This conclusion is supported by experiments demonstrating that

HeLa cells expressing human DC-SIGN (HeLa-DC-SIGN) bind exclusively to

and engulf an lgtB mutant of GC, and this interaction is blocked specifically by an anti-DC-SIGN antibody. The experiments suggest that

LOS variation may have evolved as a mechanism for GC to avoid phagocytosis by DCs.

18/7/2 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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18393065 BIOSIS NO.: 200510087565

Lipooligosaccharide-independent alteration of cellular homeostasis in
Neisseria meningitidis-infected epithelial cells

AUTHOR: Bonnahr Robert A (Reprint); Hoelter Jenny; Steeghs Liana; Enns
Caroline A; So Magdalene; Muckenthaler Martina U

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JOURNAL: Cellular Microbiology 7 (6): p869-885 JUN 05 2005

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RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Neisseria meningitidis (MC) is an important cause of meningitis and septic shock. Primary loose attachment of MC to host epithelial cells is mediated by type IV pili. Lipooligosaccharide (LOS), opacity (Opa) proteins and glycolipid adhesins facilitate subsequent tight attachment. MC infection causes numerous changes in host epithelial cell homeostasis. These include cortical plaque formation, increased expression of proinflammatory cytokines and alterations in host iron homeostasis. Using both biochemical and genetic approaches, we examined the role of LOS in mediating these events. We first examined specific cellular iron homeostasis changes that occur following addition of purified MC LOS to epithelial cells. Using an MC mutant that completely lacks LOS (MC lps tbp), we examined pili-mediated attachment and cortical plaque formation in human endocervical epithelial cells (A431). We also tested whether the lack of LOS alters cellular homeostasis, including changes in the levels of host stress response factors and proinflammatory cytokines. MC lps tbp elicited the formation of cortical plaques in A431 cells. However, the plaques were less pronounced than those formed by the MC parent. Surprisingly, the proinflammatory cytokine TNF alpha was upregulated during infection in MC lps tbp-infected cells. Furthermore, alterations in iron homeostasis, including lower transferrin receptor 1 (TfR-1) levels, altered TfR-1 trafficking, an 'iron-starvation' gene expression profile and low iron regulatory protein (IRP) binding activity are independent of LOS. Our results demonstrate that LOS is partially involved in both the attachment to host cells and formation of cortical plaques. However, TNF alpha induction and changes in iron homeostasis observed in MC-infected

epithelial cells are independent of LOS.

18/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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17135989 BIOSIS NO.: 200300094708
Lipooligosaccharide-deficient *Neisseria meningitidis* shows
altered pilus-associated characteristics.
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JOURNAL: Infection and Immunity 71 (1): p155-162 January 2003 2003
MEDIUM: print
ISSN: 0019-9567 _(ISSN print)
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RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Molecular interaction between host mucosal surfaces and
outer
membrane components of microbes is crucial in the infection
process. The
outer membrane of pathogenic *Neisseria* contains surface molecules
such as pili, PilC, and Opa and a monolayer of lipooligosaccharide
(LOS),
all of which are involved in the interaction with host cells. Pili
mediate the initial attachment to human epithelial cells, which is
followed by tight contact between bacteria and the eucaryotic cells,
leading to bacterial invasion. To further examine the basis for
bacterium-host cell contact, we constructed an LOS-deficient
Neisseria meningitidis serogroup C mutant. LOS deficiency was
without exception accompanied by altered colony opacity and
morphology, which most likely represented an "on" switch for Opa540
expression, and by reduced levels of the iron-regulated proteins
FetA and
FbpA. We show here that LOS is essential for pilus-associated
adherence
but dispensable for fiber formation and twitching motility. The
absence
of attachment to epithelial cells could not be attributed to altered
levels of piliation or defects in the pilus adhesion phenotype.
Further,
LOS mutants do not invade host cells and have lost the natural
competence
for genetic transformation.

18/7/4 (Item 4 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)
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14372127 BIOSIS NO.: 199800166374

Nonopsonic phagocytosis of group C *Neisseria meningitidis* by human neutrophils

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JOURNAL: Infection and Immunity 66 (3): p1028-1036 March, 1998 1998

MEDIUM: print

ISSN: 0019-9567

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Although complement-mediated bactericidal activity in serum has

long been known to be very important in host defense against *Neisseria meningitidis*, recent studies have shown that opsonic phagocytosis by neutrophils is also important. The purpose of this study

was to determine if endemic group C *N. meningitidis* strains were susceptible to nonopsonic (complement- and antibody-independent) phagocytosis by human neutrophils, which is a well-described phenomenon

for *Neisseria gonorrhoeae*. Gonococci that possess one or more of a group of heat-modifiable outer membrane proteins (called opacity-associated (Opa) proteins) are phagocytosed by neutrophils in the absence of serum. We found that four serogroup C meningococcal strains

bearing the lacto-N-neotetraose (LNnT) structure on lipooligosaccharide

(LOS) were phagocytosed by neutrophils in the absence of antibody and

active complement. Confocal microscopy confirmed that the organisms were

internalized by neutrophils. This susceptibility was not restricted to

carrier isolates, since two of the strains were cultured from blood or

cerebrospinal fluid. All four strains expressed Opa protein and had relatively less endogenous LOS and capsule sialylation compared to six

strains that were resistant to this type of phagocytosis. Nonopsonic phagocytosis of two of the four strains was inhibited by exogenous sialylation of LOS LNnT and the binding of monoclonal antibody to LNnT.

However, an isogenic mutant that lacked the LNnT structure was fully susceptible to nonopsonic phagocytosis. We conclude that group C

meningococci can be phagocytosed by neutrophils in the absence of antibody and active complement possibly by two different mechanisms. Expression of Opa protein and downregulation of endogenous surface sialic acids analogous to what is seen for *N. gonorrhoeae* might be necessary for *N. meningitidis* as well.

18/7/5 (Item 5 from file: 5)
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14300690 BIOSIS NO.: 199800094937

Using the yeast two-hybrid system to identify human epithelial cell proteins that bind gonococcal Opa proteins: Intracellular gonococci bind pyruvate kinase via their Opa proteins and require host pyruvate for growth

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JOURNAL: Molecular Microbiology 27 (1): p171-186 Jan., 1998 1998
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RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: *Neisseria gonorrhoeae* opacity-associated (Opa) proteins are a family of outer membrane proteins involved in gonococcal adherence to and invasion of human cells. We wanted to identify additional roles for Opa in the infectious process and used the yeast two-hybrid system to identify human epithelial cell proteins that interact with Opa proteins. Although this system has been used successfully to identify many types of interacting proteins, it has not been used to screen a human cell cDNA library for binding partners of a prokaryotic outer membrane protein. Therefore, we were also interested in exploring the versatility of the yeast two-hybrid system in identifying bacteria-host interactions. Using OpaP from strain F62SF as bait, we screened a HeLa cell cDNA library for Opa-interacting proteins (OIPs). We identified five different OIPs, designated OIP1-OIP5, two of which are homologous to human proteins - thyroid hormone receptor

interacting protein (TRIP6) and pyruvate kinase isoenzyme M2 (PK).
In the studies presented here, we investigated the interaction between

Opa proteins and PK in more depth. Opa-PK interactions were confirmed by
in vitro and in vivo assays independent of the yeast two-hybrid system.

Escherichia coli expressing six different Opa proteins from gonococcal strain FA1090 all bound more PK than Opa-negative E. coli in in vitro

binding assays. Using anti-PK antibody and fluorescence microscopy, we

showed that human epithelial cell PK co-localizes with intracellular Opa+ gonococci and E. coli expressing Opa proteins. Using a mutant of N. gonorrhoeae unable to grow on pyruvate or lactate, it appears that intracellular pyruvate is essential for gonococcal growth and survival.

These results suggest a novel mechanism in bacterial pathogenesis, i.e.

the requirement for direct molecular interaction with a host metabolic

enzyme (PK) for the acquisition of an essential intracellular carbon source and growth substrate (pyruvate). These results demonstrate that

the yeast two-hybrid system is a valuable tool for identifying biologically relevant interactions between bacteria and host proteins,

providing valuable leads for further investigations into novel mechanisms

of bacterial pathogenesis.

18/7/6 (Item 6 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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13261607 BIOSIS NO.: 199698729440

Transferrin increases adherence of iron-deprived Neisseria gonorrhoeae to human endometrial cells

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JOURNAL: American Journal of Obstetrics and Gynecology 174 (2): p659-666

1996 1996

ISSN: 0002-9378

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: OBJECTIVE: Our purpose was to study the effects of iron deprivation with and without human transferrin supplementation on the adherence and invasion of Neisseria gonorrhoeae to human endometrial cells. STUDY DESIGN: N. gonorrhoeae grown with or without iron was placed in media alone or media containing 2.5 mg/ml saturated human transferrin or unsaturated transferrin. N. gonorrhoeae was inoculated onto polarized human endometrial carcinoma cell (HEC 1-B) monolayers, and at various intervals monolayers were washed and incubated with media containing gentamicin or media alone. Colony-forming units per milliliter of N. gonorrhoeae associated with HEC 1-B cells were then determined. N. gonorrhoeae strains tested included both a transferrin receptor-positive (wild-type) and a transferrin receptor-negative mutant. Differences in percent of original inoculum remaining at varying time points were analyzed by the Mann-Whitney U test. Transmission electron microscopy using a primary endometrial cell line was used to verify findings. RESULTS: Iron-negative N. gonorrhoeae exhibited less adherence than did iron-positive N. gonorrhoeae. No difference in HEC 1-B adherence was seen when either saturated transferrin or unsaturated transferrin was added to the iron-positive N. gonorrhoeae. With iron-negative N. gonorrhoeae addition of either saturated transferrin or unsaturated transferrin significantly increased N. gonorrhoeae adherence although unsaturated transferrin did not permit growth of iron-negative N. gonorrhoeae in tissue culture media alone. Transmission electron microscopy confirmed increased adherence of iron-negative N. gonorrhoeae supplemented with unsaturated transferrin. An iron-negative N. gonorrhoeae mutant lacking the transferrin receptor exhibited no adherence regardless of addition of saturated transferrin or unsaturated transferrin. Invasion could not be quantitated reliably because of persistence of gentamicin effect. CONCLUSION: Iron and transferrin increased attachment of N. gonorrhoeae to human endometrial cells.

12944776 BIOSIS NO.: 199598412609

Adherence of Pilus- Opa+ Gonococci to Epithelial Cells In Vitro
Involves

Heparan Sulfate

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JOURNAL: Journal of Experimental Medicine 182 (2): p511-517 1995 1995

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DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Neisseria gonorrhoeae attaches to host epithelial cells via
pili and opacity-associated (Opa) outer membrane proteins. Pilus-
gonococci (Gc) of strain MS11 adhere to both human and nonhuman
Cells,

but only when particular Opa proteins are expressed; OpaA+ variants
adhere best, OpaC+ variants are next best, and the seven other Opa+
variants adhere poorly or not at all. The adherence of OpaA+ Gc to
Chinese hamster ovary (CHO) cells is inhibited by heparin or heparan
sulfate (HS), but not by chondroitin sulfate. OpaA+ Gc do not
adhere to

CHO cells devoid of HS proteoglycans; low concentrations of heparin
restore OpaA+ Gc adherence to these HS-deficient CHO cells and high
concentrations inhibit it. 3H-heparin binding to whole Gc parallels
their

adherence abilities (OpaA+ gt OpaC+ gt OpaH+ mchgt OpaB, D, E, F,
G, I

= Opa- = 0). Opa proteins separated by SDS-PAGE also bind
3H-heparin.

These data suggest that adherence of pilus-, Opa+ Gc involves
HS-proteoglycan of eukaryotic cells.

18/7/8 (Item 8 from file: 5)

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12862567 BIOSIS NO.: 199598330400

Binding of syndecan-like cell surface proteoglycan receptors is
required

for Neisseria gonorrhoeae entry into human mucosal cells

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JOURNAL: EMBO (European Molecular Biology Organization) Journal 14
(10): p

2144-2154 1995 1995

ISSN: 0261-4189

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Bacterial invasion of human mucosal cells is considered to be a primary event in the pathogenesis of a gonococcal infection. Here we report that cell surface heparan sulfate proteoglycans may play a role in the establishment of an infection, by functioning as receptors for the invasion-promoting gonococcal opacity protein adhesin. Chemical modification and enzymatic removal of proteoglycan receptors from cultured epithelial cells abolished opacity protein-associated gonococcal invasion, and mutant cell lines defective in proteoglycan synthesis were poor substrates for gonococcal attachment. The addition of purified receptor and receptor analogues totally blocked gonococcal entry into the cells. Heparin-affinity chromatography and receptor binding assays using recombinant bacteria producing defined opacity proteins and reconstituted receptor or purified receptor fragments as probes, identified one particular member of the opacity protein family (MS11-Opa-30) as the primary ligand for this novel class of receptors for bacteria. Heparan sulfate proteoglycans with gonococcal binding activity were purified from various cell types derived from target tissues of gonococcal infection, including ME-180 endocervical cells and primary cultures of human corneal epithelium. The physico-chemical properties of the receptor indicate that it may belong to the syndecan proteoglycan family.

18/7/9 (Item 9 from file: 5)
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12862190 BIOSIS NO.: 199598330023
A Lipooligosaccharide-Binding Site on HepG2 Cells Similar to the Gonococcal Opacity-Associated Surface Protein Opa
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JOURNAL: Infection and Immunity 63 (6): p2164-2172 1995 1995
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The lacto-N-neotetraose-containing lipooligosaccharide (LOS) present on the surface of most *Neisseria gonorrhoeae* organisms may serve many important functions in gonococcal pathogenesis. This surface glycolipid contains the cross-reactive epitope to human paragloboside and can be sialylated by gonococci grown in the presence of CMP-N-acetylneuraminic acid. Another possible role for this glycolipid could be to mimic human asialocarbohydrates and act as a ligand for asialoglycoprotein receptors contained on numerous human cells. The most noted of this large family of receptors is that expressed on the surface of hepatic cells. In a model cell system, using the hepatoma tissue culture cell line HepG2, we wanted to investigate if the presence of this asialoglycoprotein receptor influenced the adherence and/or invasion of gonococci expressing the lacto-N-neotetraose structure. Piliated variants of the gonococcal wild-type strain 1291 and its isogenic LOS mutant 1291E were used in adherence-invasion assays. This gonococcal strain is somewhat unusual in that it expresses large amounts of predominantly one species of LOS, thus reducing the complexity of interpreting the data. The data from these assays suggested that the Gal(beta-1-4)GlcNAc(beta-1-3)Gal(beta-1-4)Glc carbohydrate structure on the wild-type LOS affected the adherence-invasion of gonococci into the HepG2 cells. In studies to determine whether the major hepatic asialoglycoprotein receptor was involved in these interactions, we found that the HepG2 cells contained two receptors which bound gonococcal LOS. One of these was the asialoglycoprotein receptor, and the data concerning this receptor will be reported elsewhere. The data on the second receptor are reported here. Purified, ¹²⁵I-labeled gonococcal LOS was used to identify specific high-affinity LOS-binding sites. These binding experiments revealed one major binding site corresponding to a protein with a molecular mass of 70 kDa (p70). Several lines of evidence in this study suggested that the oligosaccharide region of LOS played an important role in LOS binding to the p70 of HepG2 cells. In addition, we show that this human LOS receptor has some similarities to

the gonococcal Opa proteins.

18/7/10 (Item 10 from file: 5)
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12673453 BIOSIS NO.: 199598141286
Gonococcal rfaF mutants express Rd-2 chemotype LPS and do not enter
epithelial host cells
AUTHOR: Schwan E Thomas; Robertson Brian D; Brade Helmut; Van Putten
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JOURNAL: Molecular Microbiology 15 (2): p267-275 1995 1995
ISSN: 0950-382X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have investigated the function of the Isi-1 gene of
Neisseria gonorrhoeae previously implicated in lipopolysaccharide
(LPS)-inner-core biosynthesis (Petricoin et al., 1991). Disruption
of the
gene in gonococcal strain MS11 resulted in the production of LPS
that
migrated faster than that from an isogenic galE mutant, typical for
a mutation that influences the inner-core region. Complementation
of a
panel of Salmonella typhimurium mutants with defined defects in rfa
loci
demonstrated conclusively that the Isi-1 gene of MS11 is
functionally
homologous to the rfaF gene, which encodes heptosyltransferase II
in both
E. coli and S. typhimurium. Comparison of deduced amino acid
sequences of
the gonococcal and the Salmonella RfaF demonstrated 70% similarity,
including 47% identical amino acid residues. Immunochemical
analysis of
the LPS using monoclonal antibodies directed against chemically
defined
inner-core glycoconjugates revealed that the gonococcal and
Salmonella
Rd-2-chemotypes were antigenically similar, further extending the
genetic
and functional homology. Infection experiments in vitro
demonstrated that
the Isi-1 mutant could not invade human Chang epithelial cells
despite expression of a genetically defined invasion-promoting
gonococcal

opacity protein. These data imply that the LPS phenotype is a critical factor for gonococcal invasiveness.

18/7/11 (Item 11 from file: 5)
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12308050 BIOSIS NO.: 199497329335
Interactions of Neisseria meningitidis with human monocytes
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JOURNAL: Microbial Pathogenesis 16 (2): p153-163 1994 1994
ISSN: 0882-4010
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The roles of capsule, pili and Class 5 outer-membrane proteins (Opa and Opc) of Neisseria meningitidis (Nm) in bacterial interactions with human monocytes were investigated using several meningococcal isolates of different serogroups. The presence of either Class I or Class II pili in capsulate strains of several serogroups had no significant effect on adherence to and internalisation by monocytes. Using clonal variants derived from a non-piliated serogroup A strain, C751, it was observed that capsulate bacteria (cap+) failed to interact with human monocytes in significant numbers whether or not they expressed outer-membrane proteins. These bacteria were also resistant to phagocytic killing. For capsule-deficient bacteria, expression of the Opc protein or OpaB-C751 correlated with high levels of association, while the expression of OpaDc-C751 or OpaAc-C751 resulted in comparatively lower levels. Bacteria expressing undetectable levels of Opc or Opa proteins (Opc-, Opa-) failed to interact with monocytes. In phagocytic killing assays, Opc-expressing bacteria (Opc+) as well as Opa-expressing bacteria (Opa+) were killed more readily than Opc-, Opa- bacteria (30% decrease in viability of Opc+ bacteria; 18%, 10% and 8% decrease in viability of OpaB+, OpaD+ and OpaA+ bacteria). A study of intracellular survival showed a gradual decrease in viability of both

capsulate and capsule-deficient bacteria. However, proportionately greater numbers of capsule-deficient bacteria were internalized and consequently larger numbers survived over a 4-h period. Prolonged bacterial survival within phagocytic cells may have implications in dissemination of bacteria by carriage within these cells.

18/7/12 (Item 12 from file: 5)
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11936323 BIOSIS NO.: 199396100739

Induction of immunologic memory in infants primed with Haemophilus influenzae type b conjugate vaccines

AUTHOR: Granoff D M (Reprint); Holmes S J; Osterholm M T; McHugh J E; Lucas

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JOURNAL: Journal of Infectious Diseases 168 (3): p663-671 1993

ISSN: 0022-1899

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: The ability of different Haemophilus influenzae type b conjugate

vaccines to induce immunologic memory was compared in 381 infants who

were vaccinated with one of three conjugate vaccines beginning at 2 months of age. All infants were vaccinated with unconjugated type b capsular polysaccharide, polyribosylribitol phosphate (PRP), at 12 months. In each group, high antibody responses were detected by 6-9 days

after vaccination. One month after receiving PRP, infants primed with PRP

conjugated to the outer membrane protein of Neisseria meningitidis or PRP oligomers conjugated to the cross-reactive mutant diphtheria protein, CRM-197, had twofold higher total anti-PRP antibody concentrations than did infants primed with PRP conjugated to tetanus toxoid (P lt .005). After the conjugate and the PRP

boost, notable differences were present among vaccine groups with respect

to the magnitude of the IgG anti-PRP antibody concentrations and light

chain variable region usage as determined by idiotypic analysis.

Thus,

each of the conjugate vaccines primed infants for the ability to evoke

memory antibody responses to PRP, but qualitative and quantitative

differences in priming induced by different vaccines may affect their ability to confer protection against disease.

18/7/13 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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06842283 BIOSIS NO.: 198375026226
INTERACTIONS OF NEISSERIA-GONORRHOEAE WITH HUMAN NEUTROPHILS EFFECTS
OF SERUM AND GONOCOCCAL OPACITY ON PHAGOCYTE KILLING AND CHEMI
LUMINESCENCE

AUTHOR: REST R F (Reprint); FISCHER S H; INGHAM Z Z; JONES J F
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JOURNAL: Infection and Immunity 36 (2): p737-744 1982
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Serum-sensitive strains of *N. gonorrhoeae* were incubated with suspensions of normal or chronic granulomatous disease human neutrophils in the absence or presence of fresh or heat-inactivated human serum; phagocytosis, gonococcal viability and chemiluminescence were measured. Nonpiliated opaque or transparent gonococci (colony types 3 and 4, respectively) were used for phagocytic bactericidal assays. In the presence of 2.0% fresh human serum, normal neutrophils killed > 90% of types 3 and 4 gonococci by 135 min. Serum alone at this concentration was not bactericidal. In the absence of serum, type 4 gonococci were not killed, whereas type 3 gonococci were killed to the same degree as in the presence of serum. Heat-inactivated normal serum slightly inhibited phagocytic killing of type 3 gonococci. Results almost identical to those above were obtained when 5% fresh human serum deficient in complement component 7 was substituted for 2% normal autologous serum. This indicated that the later components of complement were not involved in the observed results. To investigate the mechanisms responsible for the intracellular killing of the gonococci, neutrophils from patients with chronic granulomatous disease were used. These neutrophils are

deficient in an activable NADPH oxidase and do not produce bactericidal O₂ products upon phagocytic stimulation. Neutrophils from 2 unrelated boys with chronic granulomatous disease killed type 3 and 4 gonococci to the same degree as did normal neutrophils. As with normal neutrophils, serum was needed for killing type 4 organisms. Neutrophils from these patients showed absolutely no increased chemiluminescence in the presence of type 3 or 4 gonococci, with or without serum. The effects of serum on gonococcus-induced chemiluminescence by normal neutrophils was also investigated. In addition to type 3 and 4 gonococci, transparent colony types of lightly (type 1) and heavily (type 2) piliated organisms were also used. Chemiluminescence induced by type 1, 2 or 3 gonococci (i.e., gonococci possessing either pili or opacity-associated proteins, but not both) was augmented only slightly by serum and then only at low ratios of gonococci to neutrophils. Chemiluminescence induced by type 4 gonococci (i.e., gonococci possessing neither pili nor opacity-associated proteins) was substantially increased in the presence of serum. Stimulation of chemiluminescence by type 1, 2, 3 or 4 gonococci was dose dependent in the absence or presence of serum. Heat-killed type 3 gonococci induced chemiluminescence to the same degree as did viable organisms. Since the gonococci used in this research was strongly catalase positive, as are gonococci in general, and since it was killed by chronic granulomatous disease neutrophils, the results indicate that gonococci can be effectively killed within neutrophils, i.e., within phagolysosomes, by nonoxidative bactericidal mechanisms. Whereas type 3 gonococci were phagocytized and killed by neutrophils equally well with or without serum, serum was obligatory for phagocytic killing of type 4 gonococci, i.e., gonococci lacking opacity-associated proteins. In addition, either pili or opacity-associated proteins were apparently necessary for maximal stimulation of neutrophil chemiluminescence. The submaximal stimulation of chemiluminescence by gonococci lacking both pili and opacity-associated proteins, i.e.,

type 4 gonococci was augmented by low concentrations of nonimmune serum.

18/7/14 (Item 1 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0001517459 IP ACCESSION NO: 3775835
Adherence of pilus super(-) Opa super(+) gonococci to epithelial cells in vitro involves heparan sulfate

Chen, Tie; Belland, RJ; Wilson, J; Swanson, J*
Laboratory Microb. Struct. and Funct., Rocky Mountain Laboratory, NIAID/NIH, Hamilton, MT 59840, USA

Journal of Experimental Medicine, v 182, n 2, p 511-517, 1995
ADDL. SOURCE INFO: Journal of Experimental Medicine [J. EXP. MED.], vol. 182, no. 2, pp. 511-517, 1995
PUBLICATION DATE: 1995

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0022-1007
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

ABSTRACT:

Neisseria gonorrhoeae attaches to host epithelial cells via pili and opacity-associated (Opa) outer membrane proteins. Pilus super(-) gonococci (Gc) of strain MS11 adhere to both human and nonhuman cells, but only when particular Opa proteins are expressed; OpaA super(+) variants adhere best, OpaC super(+) variants are next best, and the seven other Opa super(+) variants adhere poorly or not at all. The adherence of OpaA super(+) Gc to Chinese hamster ovary (CHO) cells is inhibited by heparin or heparan sulfate (HS), but not by chondroitin sulfate. OpaA super(+) Gc do not adhere to CHO cells devoid of HS proteoglycans; low concentrations of heparin restore OpaA super(+) Gc adherence to these HS-deficient CHO cells and high concentrations inhibit it. super(3)H-heparin binding to whole Gc parallels their adherence abilities (OpaA super(+) > OpaC super(+) > OpaH super(+) >> OpaB, D, E, F, G, I = Opa super(-) = 0). Opa proteins

separated by SDS-PAGE also bind super(3)H-heparin. These data suggest that adherence of pilus super(-), Opa super(+) Gc involves HS-proteoglycan of eukaryotic cells.

18/7/15 (Item 2 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0001506491 IP ACCESSION NO: 3762664
Gonococcal opacity: Lectin-like interactions between Opa proteins and lipooligosaccharide

Blake, MS; Blake, CM; Apicella, MA; Mandrell, RE
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Infection and Immunity, v 63, n 4, p 1434-1439, 1995
ADDL. SOURCE INFO: Infection and Immunity [INFECT. IMMUN.], volume 63, number 4, pp. 1434-1439, 1995
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SUMMARY LANGUAGE: English
ISSN: 0019-9567
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

ABSTRACT:

Previous evidence from our laboratory suggested that the tight intercellular adhesions between the outer membranes of gonococci displaying the opacity colony phenotype occurred because Opa proteins expressed on one gonococcus adhered to the lipooligosaccharide (LOS) of the opposing bacterium. A noncompetitive inhibition assay used previously to determine the carbohydrate structures recognized by the major hepatic asialoglycoprotein receptor was modified to determine the gonococcal LOS structures that bind Opa proteins. The LOS carbohydrates used in these assays were LOS structures purified from pyocin LOS mutants of *Neisseria gonorrhoeae* 1291 described by K. C. Dudas and M. A. Apicella and further characterized by C. M. John et al. Purified gonococcal Opa proteins were incubated with each of the parent and mutant LOS, and the amount of binding of Opa proteins was measured by a direct enzyme-linked immunosorbent assay using the Opa-specific monoclonal antibody 4B12. The affinities of the Opa proteins for each of the LOS were

determined indirectly by measuring the concentrations of Opa proteins that noncompetitively inhibited 50% of the binding of LOS-specific monoclonal antibodies. This concentration is inversely proportional to the affinity of the inhibitor. Our data suggest that the gonococcal Opa proteins tested had the highest affinity for the Gal beta 1-4GlcNAc residue present on the gonococcal lactoneoseries LOS. This affinity was comparable to that reported for the binding of the major hepatic asialoglycoprotein receptor to glycoconjugates containing terminal galactose and N-acetylgalactosamine. After sialylation of the lactoneoseries LOS, presumably on the terminal galactose residue, the interaction with the Opa proteins was ablated. Therefore, the gonococcal Opa-LOS and mammalian epithelial cell asialoglycoprotein receptor-carbohydrate interactions have quite similar specificities.

18/7/16 (Item 3 from file: 24)
DIALOG(R)File 24:CSA Life Sciences Abstracts
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0001464509 IP ACCESSION NO: 3707095
Gonococcal rfaF mutants express Rd sub(2) chemotype LPS and do not enter epithelial host cells

Schwan, ET; Robertson, BD; Brade, H; Van Putten, JPM*
Max-Planck-Inst. Biol., Abt. Infektionsbiol., Spemannstrasse 34, D 72076
Tuebingen, FRG

Molecular Microbiology, v 15, n 2, p 267-275, 1995
ADDL. SOURCE INFO: Molecular Microbiology [MOL. MICROBIOL.], volume 15, number 2, pp. 267-275, 1995
PUBLICATION DATE: 1995

DOCUMENT TYPE: Journal Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ISSN: 0950-382X
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

ABSTRACT:

We have investigated the function of the Isi-1 gene of Neisseria

gonorrhoeae previously implicated in lipopolysaccharide (LPS)-inner-core biosynthesis (Petricoin et al., 1991). Disruption of the gene in gonococcal strain MS11 resulted in the production of LPS that migrated faster than that from an isogenic galE mutant, typical for a mutation that influences the inner-core region. Complementation of a panel of Salmonella typhimurium mutants with defined defects in rfa loci demonstrated conclusively that the Isi-1 gene of MS11 is functionally homologous to the rfaF gene, which encodes heptosyltransferase II in both E. coli and S. typhimurium. Comparison of deduced amino acid sequences of the gonococcal and the Salmonella RfaF demonstrated 70% similarity, including 47% identical amino acid residues. Immunochemical analysis of the LPS using monoclonal antibodies directed against chemically defined inner-core glycoconjugates revealed that the gonococcal and Salmonella Rd sub(2)-chemotypes were antigenically similar, further extending the genetic and functional homology. Infection experiments in vitro demonstrated that the Isi-1 mutant could not invade human Chang epithelial cells despite expression of a genetically defined invasion-promoting gonococcal opacity protein. These data imply that the LPS phenotype is a critical factor for gonococcal invasiveness.

18/7/17 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

18350701 Genuine Article#: 352VS Number of References: 67
Title: Clinically relevant mutations that cause derepression of the Neisseria gonorrhoeae MtrC-MtrD-MtrE efflux pump system confer different levels of antimicrobial resistance and in vivo fitness
Author(s): Warner DM; Shafer WM; Jerse AE (REPRINT)
Corporate Source: Uniformed Serv Univ Hlth Sci, F Edward Hebert Sch Med,
Dept Microbiol & Immunol, Bethesda//MD/20814 (REPRINT); Uniformed Serv Univ Hlth Sci, F Edward Hebert Sch Med, Dept Microbiol & Immunol, Bethesda//MD/20814; Emory Univ, Sch Med, Dept Microbiol & Immunol, Atlanta//GA/30322; Vet Affairs Med Ctr, VA Med Res Serv, Labs
Microbial Pathogenesis, Decatur//GA/30033
Journal: MOLECULAR MICROBIOLOGY, 2008, V70, N2 (OCT), P462-478
ISSN: 0950-382X Publication date: 20081000
Publisher: BLACKWELL PUBLISHING, 9600 GARSINGTON RD, OXFORD OX4 2DQ, OXON,

ENGLAND

Language: English Document Type: ARTICLE

Abstract: The MtrC-MtrD-MtrE efflux pump system confers resistance to macrolide antibiotics and antimicrobial substances of the host innate

defence. Clinical isolates with increased resistance to erythromycin

and azithromycin frequently harbour mutations in the mtrR structural

gene, which encodes a repressor of the mtrCDE operon, or the mtrR promoter region. The MtrC-MtrD-MtrE system is important for gonococcal

survival in the murine genital tract, and derepression of the mtrCDE

operon via deletion of mtrR confers increased fitness in vivo.

Here we compared isogenic strains with naturally occurring mtrR locus

mutations for differences in mtrCDE expression and pump-related phenotypes. Mutations upstream of mtrC, including those within the MtrR

binding region and a novel mutation that increases mtrC RNA stability

conferred the highest levels of derepression as measured by mtrCDE transcription and resistance to antibiotics, progesterone and antimicrobial peptides. In contrast, mutations within the mtrR

coding

sequence conferred low to intermediate levels of derepression. In

vivo,

the mtr mutants were more fit than the wild-type strain, the degree to

which paralleled in vitro resistance gradients. These studies establish

a hierarchy of mtrR locus mutations with regard to regulation of pump

efflux, and suggest selection for more derepressed mutants may occur

during mixed infections.

18/7/18 (Item 2 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

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16772165 Genuine Article#: 194PB Number of References: 48

Title: Opa proteins of pathogenic Neisseriae initiate src

kinase-dependent

or lipid raft-mediated uptake via distinct human carcinoembryonic antigen-related cell adhesion molecule isoforms

Author(s): Schmitter T; Pils S; Weibel S; Agerer F; Peterson L; Buntru A;

Kopp K; Hauck CR (REPRINT)

Corporate Source: Univ Konstanz, Lehrstuhl Zellbiol, Postfach X908/D-78457

Constance//Germany/ (REPRINT); Univ Konstanz, Lehrstuhl
Zellbiol, D-78457

Constance//Germany//; Univ Wurzburg, Zentrum Infekt
Forschung, D-97070

Wurzburg//Germany/

Journal: INFECTION AND IMMUNITY, 2007, V75, N8 (AUG), P4116-4126

ISSN: 0019-9567 Publication date: 20070800

Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC
20036-2904

USA

Language: English Document Type: ARTICLE

Abstract: Several pathogenic bacteria exploit human carcinoembryonic
antigen-related cell adhesion molecules (CEACAMs) for adhesion to
and

invasion into their host cells. CEACAM isoforms have
characteristic

expression patterns on epithelial, endothelial, or hematopoietic
cells,

providing bacteria with distinct sets of receptors on particular
tissues. For example, while CEACAM1 and CEACAM6 have a wide tissue
distribution, CEACAM3, CEACAM4, and CEACAM8 are uniquely

expressed on

primary human granulocytes, whereas CEA and CEACAM7 are limited to
epithelia. By reconstitution of a CEACAM-deficient cell line with
individual CEACAMs, we have analyzed the requirements for
CEACAM-mediated internalization of *Neisseria gonorrhoeae*. Our
results point to two mechanistically different uptake pathways
triggered by either epithelial CEACAMs (CEACAM1, CEA, and
CEACAM6) or

the granulocyte-specific CEACAM3. In particular, CEACAM3-mediated
uptake critically depends on Src family protein tyrosine kinase
(PTK) activity, and CEACAM3 associates with the SH2 domains of
several

Src PTKs. In contrast, epithelial CEACAMs require the integrity of
cholesterol-rich membrane microdomains and are affected by

cholesterol
depletion, whereas CEACAM3-mediated uptake by transfected cells

or the
opsonin-independent phagocytosis by human granulocytes is not

altered
in the presence of cholesterol chellators. These results allow the
subdivision of all human CEACAMs known to be utilized as pathogen
receptors into functional groups and point to important
consequences

for bacterial engagement of distinct CEACAM isoforms.

18/7/19 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

10493393 Genuine Article#: 534FE Number of References: 43

Title: Carcinoembryonic antigen family receptor recognition by gonococcal

Opa proteins requires distinct combinations of hypervariable Opa protein domains

Author(s): Bos MP (REPRINT) ; Kao D; Hogan DM; Grant CCR; Belland RJ
Corporate Source: Univ Utrecht, Dept Mol Microbiol, Padualaan 8/NL-3584 CH

Utrecht//Netherlands/ (REPRINT); NIAID, Rocky Mt Lab, Lab Human Bacterial Pathogenesis, NIH, Hamilton//MT/59840

Journal: INFECTION AND IMMUNITY, 2002, V70, N4 (APR), P1715-1723

ISSN: 0019-9567 Publication date: 20020400

Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904

USA

Language: English Document Type: ARTICLE

Abstract: Neisserial Opa proteins function as a family of adhesins that

bind heparan sulfate proteoglycan (HSPG) or carcinoembryonic antigen

family (CEACAM) receptors on human host cells. In order to define the

CEACAM binding domain on Opa proteins, we tested the binding properties

of a series of gonococcal (strain MS11) recombinants producing mutant and chimeric Opa proteins with alterations in one or more of the four surface-exposed loops. Mutagenesis demonstrated that

the

semivariable domain, present in the first loop, was completely dispensable for CEACAM binding. In contrast, the two

hypervariable (HV)

regions present in the second and third loops were essential for binding; deletion of either domain resulted in loss of receptor recognition. Deletion of the fourth loop resulted in a severe decrease in Opa expression at the cell surface and could

therefore not

be tested for CEACAM binding. Chimeric Opa variants, containing combinations of RV regions derived from different CEACAM binding

Opa

proteins, lost most of their receptor binding activity. Some chimeric

variants gained HSPG binding activity. Together, our results indicate

that full recognition of CEACAM receptors by Opa proteins

requires a

highly coordinate interplay between both HV regions. Furthermore, shuffling of HV regions may result in novel HSPG receptor binding activity.

10402048 Genuine Article#: 522EQ Number of References: 52
Title: Interaction of an outer membrane protein of enterotoxigenic
Escherichia coli with cell surface heparan sulfate proteoglycans
Author(s): Fleckenstein JM (REPRINT) ; Holland JT; Hasty DL
Corporate Source: Vet Affairs Med Ctr, Res Serv 151, 1030 Jefferson
Ave/Memphis//TN/38104 (REPRINT); Vet Affairs Med Ctr, Res Serv
151, Memphis//TN/38104; Vet Affairs Med Ctr, Med
Serv, Memphis//TN/38104;
Univ Tennessee, Dept Med, Memphis//TN/38163; Univ Tennessee, Dept
Anat, Memphis//TN/38163
Journal: INFECTION AND IMMUNITY, 2002, V70, N3 (MAR), P1530-1537
ISSN: 0019-9567 Publication date: 20020300
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC
20036-2904
USA

Language: English Document Type: ARTICLE

Abstract: We have previously shown that enterotoxigenic invasion
protein A (Tia), a 25-kDa outer membrane protein encoded on
an apparent pathogenicity island of enterotoxigenic Escherichia
coli

(ETEC) strain H10407, mediates attachment to and invasion into
cultured
human gastrointestinal epithelial cells. The epithelial cell
receptor(s) for Tia has not been identified. Here we show that Tia
interacts with cell surface heparan sulfate proteoglycans.

Recombinant

E. coli expressing Tia mediated invasion into wild-type
epithelial cell
lines but not invasion into proteoglycan-deficient cells.
Furthermore, wild-type eukaryotic cells, but not proteoglycan-
deficient eukaryotic cells, attached to immobilized
polyhistidine-tagged recombinant Tia (rTia). Binding of epithelial
cells to immobilized rTia was inhibited by exogenous heparan
sulfate

glycosaminoglycans but not by hyaluronic acid, dermatan sulfate,
or
chondroitin sulfate. Similarly, pretreatment of eukaryotic cells
with

heparinase 1, but not pretreatment of eukaryotic cells with
chondroitinase ABC, inhibited attachment to rTia. In addition,
we also

observed heparin binding to both immobilized rTia and recombinant
E.

coli expressing Tia. Heparin binding was inhibited by a synthetic
peptide representing a surface loop of Tia, as well as by
antibodies

directed against this peptide. Additional studies indicated that
Tia,

as a prokaryotic heparin binding protein, may also interact via
sulfated proteoglycan molecular bridges with a number of mammalian
heparan sulfate binding proteins. These findings suggest that the

binding of Tia to host epithelia] cells is mediated at least in part through heparan sulfate proteoglycans and that ETEC belongs on the growing list of pathogens that utilize these ubiquitous cell surface molecules as receptors.

18/7/21 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

09942529 Genuine Article#: 467DH Number of References: 71
Title: Homophilic adhesion of human CEACAM1 involves N-terminal domain interactions: structural analysis of the binding site
Author(s): Watt SM (REPRINT) ; Teixeira AM; Zhou GQ; Doyonnas R; Zhang Y;
Grunert F; Blumberg RS; Kuroki M; Skubitz KM; Bates PA
Corporate Source: John Radcliffe Hosp, Natl Blood Serv, Stem Cell Lab, Oxford
OX3 9DS//England/ (REPRINT); Natl Blood Serv, Stem Cell Lab, Nuffield
Dept clin & Lab Sci, Oxford//England/; MRC, Mol Haematol Unit, Inst Mol
Med, Oxford//England/; Univ Coimbra, Fac Ciencias Desporto & Educ Fis, Coimbra//Portugal/; GENOVAC AG, Freiburg//Germany/; Harvard Univ, Sch
Med, Brigham & Womens Hosp, Div Gastroenterol, Boston//MA/; Fukuoka Univ, Sch Med, Dept Biochem, Fukuoka 81401//Japan/; Univ Minnesota, Sch
Med, Minneapolis//MN/55455; Imperial Canc Res Fund, Biomolec Modelling
Lab, London//England/
Journal: BLOOD, 2001, V98, N5 (SEP 1), P1469-1479
ISSN: 0006-4971 Publication date: 20010901
Publisher: AMER SOC HEMATOLOGY, 1900 M STREET. NW SUITE 200, WASHINGTON, DC
20036 USA
Language: English Document Type: ARTICLE
Abstract: CEACAM1 on leukocytic, endothelial, and epithelial cells functions in homophilic adhesion, tumor suppression, regulating cell adhesion and proliferation, and in heterophilic adhesion as a receptor for E-selectin and Neisseria meningitidis, Neisseria gonorrhoeae, Haemophilus influenzae, and murine coronaviruses.
The 8 transmembrane isoforms of human CEACAM1 possess an extracellular N-terminal IgV domain, followed by variable numbers of IgC2 domains. To establish which key amino acids contribute specifically to CEACAM1 homophilic adhesion, exposed amino acids in the N-terminal domain of a

soluble form of CEACAM1 were subjected to mutagenesis. Analyses of mutant proteins with conformationally dependent antibodies indicated that most mutations did not substantially affect the structural integrity of CEACAM1. Nevertheless, decreased adhesion was observed for the single mutants V39A or D40A (single-letter amino acid codes) in the CC ' loop and for the triple mutants located in the GFCC 'C " face of the N-terminal domain. Interestingly, whereas single mutations in R64 or D82 that are predicted to form a salt bridge between the base of the D and F beta strands close to the critical V39 and D40 residues also abolish adhesion, an amino acid swap (R64D and D82R), which maintains the salt bridge was without significant effect. These studies indicate that the CC ' loop plays a crucial role in the homophilic adhesion of CEACAM1. They further predict that specific hydrophobic amino acid residues on the nonglycosylated GFCC 'C " face of CEACAM1 N-terminal domain are not only involved in heterophilic interactions with Opa proteins and H influenzae, but are also critical for protein-protein interactions between 2 CEACAM1 molecules on opposing cells. (C) 2001 by The American Society of Hematology.

18/7/22 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

08357326 Genuine Article#: 275VZ Number of References: 64
Title: Isolation of Neisseria gonorrhoeae mutants that show enhanced trafficking across polarized T84 epithelial monolayers
Author(s): Hopper S (REPRINT) ; Wilbur JS; Vasquez BL; Larson J; Clary S; Mehr IJ; Seifert HS; So M
Corporate Source: OREGON HLTH SCI UNIV,DEPT MOL MICROBIOL & IMMUNOL, L220, 3181 SW SAM JACKSON RD/PORTLAND//OR/97201 (REPRINT); NORTHWESTERN UNIV,SCH MED, DEPT MICROBIOL IMMUNOL/CHICAGO//IL/60611
Journal: INFECTION AND IMMUNITY, 2000, V68, N2 (FEB), P896-905
ISSN: 0019-9567 Publication date: 20000200
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
Language: English Document Type: ARTICLE
Abstract: Initiation of a gonococcal infection involves attachment of Neisseria gonorrhoeae to the plasma membrane of an epithelial cell in the mucosal epithelium and its internalization, transepithelial

trafficking, and exocytosis from the basal membrane. Piliation and expression of certain Opa proteins and the immunoglobulin A1 protease influence the transcytosis process. We are interested in identifying other genetic determinants of *N. gonorrhoeae* that play a role in transcellular trafficking. Using polarized T84 monolayers as a model epithelial barrier, we have assayed an *N. gonorrhoeae* FA1090 minitransposon (mTn) mutant bank for isolates that traverse the monolayer more quickly than the isogenic wild-type (WT) strain. From an initial screen, we isolated four mutants, defining three genetic loci, that traverse monolayers significantly more quickly than their WT parent strain. These mutants adhere to and invade cells normally and do not affect the integrity of the monolayer barrier. Backcrosses of the mutations into the WT FA1090 strain yielded mutants with a similar fast-trafficking phenotype. In two mutants, the mTns had inserted 370 bp apart into the same locus, which we have named *fit*, for fast intracellular trafficker. Backcrosses of one of these mutants into the MS11A genetic background also yielded a fast-tracking mutant. The *fit* locus contains two overlapping open reading frames, *fitA* and *fitB*, whose deduced amino acid sequences have predicted molecular weights of 8.6 and 15.3, respectively. Neither protein contains a signal sequence. *FitA* has a potential helix-turn-helix motif, while the deduced sequence of *FitB* offers no clues to its function. *fitA* or *fitB* homologues are present in the genomes of *Pseudomonas syringae* and *Rhizobium meliloti*, but not *Neisseria meningitidis*. Replication of the MS11A *fitA* mutant in A431 and T84 cells is significantly accelerated compared to that of the isogenic WT strain. In contrast, growth of this mutant in Liquid media is normal. Taken together, these results strongly suggest that traversal of *N. gonorrhoeae* across an epithelial barrier is linked to intracellular bacterial growth.

18/7/23 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

07647998 Genuine Article#: 191RE Number of References: 47
Title: Proteoglycan receptor binding by *Neisseria gonorrhoeae* MS11 is determined by the HV-1 region of OpaA

Author(s): Grant CCR; Bos MP; Belland RJ (REPRINT)
Corporate Source: NIAID, MICROBIAL STRUCT & FUNCT LAB, ROCKY MT LABS,
903 S

4TH ST/HAMILTON//MT/59840 (REPRINT); NIAID, MICROBIAL STRUCT &
FUNCT

LAB, ROCKY MT LABS/HAMILTON//MT/59840

Journal: MOLECULAR MICROBIOLOGY, 1999, V32, N2 (APR), P233-242

ISSN: 0950-382X Publication date: 19990400

Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2
ONE,

OXON, ENGLAND

Language: English Document Type: ARTICLE

Abstract: The interaction of the OpaA protein of Neisseria
gonorrhoeae MS11mk with heparan sulphate-containing proteoglycan
receptors on Chang conjunctiva epithelial cells was examined using
isolated receptor binding and cell adherence/internalization
assays.

OpaA deletion proteins, in which the four surface-exposed regions
of the protein were deleted individually, and chimeric OpaA/B
proteins, in which the surface-exposed regions of the OpaA and

OpaB
proteins were exchanged, were expressed in N. gonorrhoeae. The
recombinant deletion proteins and the chimeric OpaA/B proteins
were surface exposed in the outer membrane of N. gonorrhoeae.

Isolated
receptor-binding assays and Chang cell infection assays with OpaA
deletion variants indicated that hypervariable region 1 was
essential for the interaction of N. gonorrhoeae with the

proteoglycan
receptor. Expression of chimeric OpaA/B proteins confirmed the
central

role of hypervariable region 1 in receptor binding and
demonstrated

that this domain alone confers the invasive biological phenotype
in a

non-heparan sulphate proteoglycan-binding Cpa protein. The other
variable regions of OpaA enhanced receptor binding in the
presence of

region 1, but did not constitute binding domains on their own. The
results indicate that proteoglycan receptor binding results from a
hierarchical interaction between the variable domains of the OpaA
protein of MS11mk.

18/7/24 (Item 8 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

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06958700 Genuine Article#: 108BR Number of References: 38

Title: CD66 receptor specificity exhibited by neisserial Opa variants
controlled by protein determinants in CD66 N-domains

Author(s): Bos MP (REPRINT) ; Kuroki M; KropWatorek A; Hogan D;
Belland RJ

Corporate Source: NIAID, ROCKY MT LABS, LAB MICROBIAL STRUCT & FUNCT,
NIH,
903 S 4TH ST/HAMILTON//MT/59840 (REPRINT); FUKUOKA UNIV, SCH MED,
DEPT
BIOCHEM 1/FUKUOKA 81401//JAPAN//; POLISH ACAD SCI, INST IMMUNOL &
EXPT
THERAPY, DEPT IMMUNOCHEM/PL-53114 WROCLAW//POLAND/
Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED
STATES OF AMERICA, 1998, V95, N16 (AUG 4), P9584-9589
ISSN: 0027-8424 Publication date: 19980804
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON,
DC

20418

Language: English Document Type: ARTICLE

Abstract: Neisseria gonorrhoeae strain MS11 is able to express 11
different opacity (Opa) proteins on its outer surface. A number
of these Opa proteins have been shown to function as adhesins
through
binding of CD66 receptors present on human cells. CD66 antigens,
or
carcinoembryonic antigen family members, constitute a family of
glycoproteins belonging to the immunoglobulin superfamily. Opa
variants
recognize this class of receptors in a differential manner such
that
certain Opa variants recognize up to four different CD66 receptors
(CD66a, -c, -d, and -e), whereas others recognize only two (CD66a
and
-e) or none. We explored the basis for this receptor tropism in
the
present study. Our data show that glycoforms of CD66e and
deglycosylated CD66e are recognized by gonococci in an
Opa-specific
manner. Binding by Opa variants of recombinant N-terminal domains
of
CD66 receptors expressed in Escherichia coli reflected the
adherence
specificities of Opa variants to HeLa cells expressing native CD66
molecules. These data indicate that recognition of CD66 receptors
by
Opa variants is mediated by the protein backbone of the CD66
N-domains. Furthermore, by using chimeric constructs between
different
CD66 N-domains we identified distinct binding regions on the CD66e
N-domain for specific groups of Opa variants, suggesting that the
differential recognition of CD66 receptors by Opa variants is
dictated
by the presence of specific binding regions on the N-domain of the
receptor.

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2009 The Thomson Corp. All rts. reserv.

03993948 Genuine Article#: QX649 Number of References: 40

Title: PHENOTYPIC VARIATION IN HAEMOPHILUS-INFLUENZAE - THE
INTERRELATIONSHIP OF COLONY OPACITY, CAPSULE AND
LIPOPOLYSACCHARIDE

Author(s): ROCHE RJ; MOXON ER

Corporate Source: JOHN RADCLIFFE HOSP, INST MOLEC MED, DEPT
PAEDIAT, MOLEC

INFECT DIS GRP/OXFORD OX3 9DU//ENGLAND/

Journal: MICROBIAL PATHOGENESIS, 1995, V18, N2 (FEB), P129-140

ISSN: 0882-4010

Language: ENGLISH Document Type: ARTICLE

Abstract: H. influenzae type b strains show phase variation between
opaque

(O) and translucent (T) colony phenotypes. These phenotypic
differences

have been related to differences in virulence for infant rats.

This

study shows that the switch between O and T colony phenotypes is
associated with variation in the amount of cell-associated
capsule in

the serotype b strains Rd:b+:01, RM7004 and Eagan. O colonies
comprised

organisms which were more serum resistant and had more
cell-associated

polyribosyl ribitol phosphate (PRP) than organisms from T
colonies.

Strain Rd, the non-encapsulated parent of the encapsulated
transformant

Rd:b+:01, was constitutively translucent, consistent with its
lack of
capsule expression.

Since previous studies had correlated O-T switching with
differences in the relative molecular weight of lipopolysaccharide
(LPS), LPS phenotypes of Rd and Rd : b+:01 were compared and
correlated

with opacity phenotype at the individual colony level. Both
strains showed phase variation between higher and lower molecular
weight LPS oligosaccharide structures but the prevalence of higher
molecular weight LPS was greater for the capsule-deficient Rd
than encapsulated Rd:b+:01. Capsule-deficient mutants of strains
Rd:b+:01, RM7004 and Eagan produced constitutively translucent
colonies

and each had a greater prevalence of higher molecular weight LPS
than

their encapsulated parents. These findings indicated an incomplete
association between capsular O-T phase variation and LPS
expression.

18/7/26 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02443362 Genuine Article#: LB800 Number of References: 37
Title: ROUGH MORPHOLOGICAL VARIANTS OF MYCOBACTERIUM-AVIUM -
CHARACTERIZATION OF GENOMIC DELETIONS RESULTING IN THE LOSS OF
GLYCOPEPTIDOLIPID EXPRESSION
Author(s): BELISLE JT; KLACZKIEWICZ K; BRENNAN PJ; JACOBS WR; INAMINE
JM
Corporate Source: COLORADO STATE UNIV,DEPT MICROBIOL/FT
COLLINS//CO/80523;
COLORADO STATE UNIV,DEPT MICROBIOL/FT COLLINS//CO/80523; YESHIVA
UNIV
ALBERT EINSTEIN COLL MED,HOWARD HUGHES MED INST/BRONX//NY/10461;
YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT MICROBIOL &
IMMUNOL/BRONX//NY/10461
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 1993, V268, N14 (MAY 15), P
10517-10523
ISSN: 0021-9258
Language: ENGLISH Document Type: ARTICLE
Abstract: Previously, a gene cluster, termed ser2, which encodes for
the
synthesis of the specific oligosaccharide of the glycopeptidolipid
antigen of Mycobacterium avium serovar 2 strain TMC 724, was
defined.
DNA probes from this cloned ser2 gene cluster have now been used
to
clone and characterize the ser2 region from a strain of M. avium
which
produces rough and smooth colony forms and to identify the genetic
differences between these morphotypes. Interstrain differences
were
seen to exist between the ser2 gene cluster of M. avium strains
TMC 724
and 2151. In addition, two distinct rough (Rg) genotypes of
strain 2151
were defined by this analysis. The first of these, present in the
M.
avium Rg-0 and Rg-1 variants, was attributed to a deletion of
approximately 28 kilobases from smooth variants, including the
entire
ser2 gene cluster. This particular deletion is thought to be
mediated by recombination between repetitive sequences that flank
both
sides of the 28-kilobase excised region. The second genotype,
seen in
M. avium Rg-3 and Rg-4 variants, results from the deletion of an
undefined amount of DNA from the right of the ser2 gene cluster.
Reported separately (Belisle, J. T., McNeil, M. R., Chatterjee,
D.,
Inamine, J. M., and Brennan, P. J. (1993) J. Biol. Chemical 268,

10510-10516) are the results of biochemical analyses of the glycopeptidolipid/lipopeptide population of the Rg genotypes which revealed that Rg-0 and Rg-1 possess lipopeptides devoid of all of the sugars of the glycopeptidolipids and are obviously biosynthetic precursors of the glycopeptidolipids. These studies help formulate a definition of the physiological effects of glycolipid expression, the biosynthetic and genetic mechanisms involved in their formation, and toward an understanding of the role of *M. avium* as a serious opportunistic pathogen.

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Phase and antigenic variation mediated by genome modifications
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Phase and antigenic variation is used by several bacterial species to generate intra-population diversity that increases bacterial fitness and is important in niche adaptation, or to escape host defences. By this adaptive process, bacteria undergo frequent and usually reversible phenotypic changes resulting from genetic or epigenetic alterations at specific genetic loci. Phase variation or phenotypic switch allows the expression of a given phenotype to be switched ON or OFF. Antigenic variation refers to

the expression of a number of alternative forms of an antigen on the cell surface, and at a molecular level, shares common features with phase variation mechanisms. This review will focus on phase and antigenic variation mechanisms implying genome modifications, with an emphasis on the diversity of phenotypes regulated by these mechanisms, and the ecological relevance of variant appearance within a given population. (c) Springer Science+Business Media B.V. 2008.

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AmiC functions as an N-acetylmuramyl-L-alanine amidase necessary for cell separation and can promote autolysis in *Neisseria gonorrhoeae*
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Neisseria gonorrhoeae is prone to undergo autolysis under many conditions not conducive to growth. The role of autolysis during gonococcal infection is not known, but possible advantages for the bacterial population include provision of nutrients to a starving population, modulation of the host immune response by released cell components, and donation of DNA for natural transformation. Biochemical studies indicated that an N-acetylmuramyl-L-alanine amidase is responsible for cell wall breakdown during autolysis. In order to better understand autolysis and in

hopes of creating a nonautolytic mutant, we mutated *amiC*, the gene for a putative peptidoglycan-degrading amidase in *N. gonorrhoeae*. Characterization of peptidoglycan fragments released during growth showed that an *amiC* mutant did not produce free disaccharide, consistent with a role for *AmiC* as an N-acetylmuramyl-L-alanine amidase. Compared to the wild-type parent, the mutant exhibited altered growth characteristics, including slowed exponential-phase growth, increased turbidity in stationary phase, and increased colony opacity. Thin-section electron micrographs showed that mutant cells did not fully separate but grew as clumps. Complementation of the *amiC* deletion mutant with wild-type *amiC* restored wild-type growth characteristics and transparent colony morphology. Overexpression of *amiC* resulted in increased cell lysis, supporting *AmiC*'s purported function as a gonococcal autolysin. However, *amiC* mutants still underwent autolysis in stationary phase, indicating that other gonococcal enzymes are also involved in this process. Copyright (c) 2006, American Society for Microbiology. All Rights Reserved.

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Critical determinants of host receptor targeting by *Neisseria meningitidis* and *Neisseria gonorrhoeae*: Identification of Opa adhesiotopes on the N-domain of CD66 molecules
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The human pathogens *Neisseria meningitidis* and *Neisseria gonorrhoeae* express a family of variable outer membrane opacity-associated (Opa) proteins that recognize multiple human cell surface receptors. Most Opa proteins target the highly conserved N-terminal domain of the CD66 family of adhesion molecules, although a few also interact with heparan sulphate proteoglycans. In this study, we observed that at least two Opa proteins of a *N. meningitidis* strain C751 have the dual capacity to interact with both receptors. In addition, all three Opa proteins of C751 bind equally well to HeLa cells transfected with cDNA encoding the carcinoembryonic antigen [CEA (CD66e)] subgroup of the CD66 family, but show distinct tropism for CGM1-(CD66d) and NCA (CD66c)-expressing cells. Because the C751 Opa proteins make up distinct structures via the surface-exposed hypervariable domains (HV-1 and HV-2), these combinations appear to be involved in tropism for the distinct CD66 subgroups. To define the determinants of receptor recognition, we used mutant proteins of biliary glycoprotein [BGP (CD66a)] carrying substitutions at several predicted exposed sites in the N-domain and compared their interactions with several Opa proteins of both *N. meningitidis* and *N. gonorrhoeae*. The observations applied to the molecular model of the BGP N-domain that we constructed show that the binding of all Opa proteins tested occurs at the non-glycosylated (CFG) face of the molecule and, in general, appears to require Tyr-34 and Ile-91. Further, efficient interaction of distinct Opa proteins depends on different non-adjacent amino acids. In the three-dimensional model, these residues lie in close proximity to Tyr-34 and Ile-91 at the CFG face, making continuous binding domains (adhesiotopes). The epitope of the monoclonal antibody YTH71.3 that inhibits Opa/CD66 interactions was also identified within the Opa adhesiotopes on the N-domain. These studies define the molecular basis that directs the Opa specificity for the CD66 family and the rationale for tropism of the Opa proteins for the CD66 subgroups.

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Exploitation of Mammalian Host Cell Functions by Bacterial Pathogens
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Abstract: Interest in bacterial pathogenesis has recently increased because of antibiotic resistance, the emergence of new pathogens and the resurgence of old ones, and the lack of effective therapeutics. The molecular and cellular mechanisms of microbial pathogenesis are currently being defined, with precise knowledge of both the common strategies used by multiple pathogenic bacteria and the unique tactics evolved by individual species to help establish infection. What is emerging is a new appreciation of how bacterial pathogens interact with host cells. Many host cell functions, including signal transduction pathways, cytoskeletal rearrangements, and vacuolar trafficking, are exploited, and these are the focus of this review. A bonus of this work is that bacterial virulence factors are providing new tools to study various aspects of mammalian cell functions, in addition to mechanisms of bacterial disease. Together these developments may lead to new therapeutic strategies.

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